

# The Learning Brain

Edited by  
E. A. ASRATYAN and P. V. SIMONOV

Advances  
in  
Science  
and  
Technology  
in  
the USSR



Medical Series

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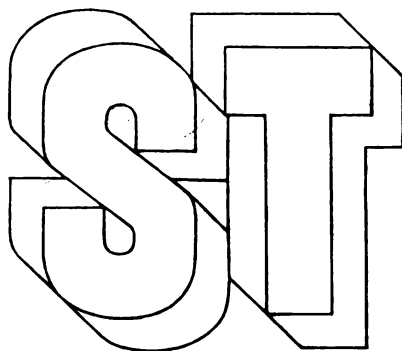




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# The Learning Brain .

Edited by

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## Обучающийся мозг

Под редакцией  
чл.-корр. АН СССР  
*Э. А. Асратяна*  
и чл.-корр. АН СССР  
*П. В. Симонова*

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## FOREWORD

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This book presents the findings of research carried out at the Institute of Higher Nervous Activity and Neurophysiology (USSR Academy of Sciences), the thirtieth anniversary of whose founding was celebrated in 1980. The contributors include both leading Soviet scientists whose names are familiar to the scientific public, like the late E. A. Asratyan, Member of the Armenian Academy of Sciences and Corresponding Member of the USSR Academy of Sciences, M. N. Livanov, Member of the USSR Academy of Sciences, V. S. Rusinov, Member of the USSR Academy of Medical Sciences, and the middle generation of Soviet neurophysiologists, heads of the Institute's laboratories.

The papers are linked by the common theoretical position of their authors who, basing themselves on the works of Sechenov, Pavlov, and Ukhtomsky, the fathers of Soviet physiology, have employed the broad arsenal of modern experimental technique and mathematical data processing.

The general theme is the physiological mechanisms of learning and memory, i.e. the processes of the development, retention and realization of conditioned reflexes. The conditioned reflex, though a central phenomenon in higher nervous activity, does not, by itself, ensure purposeful behaviour. Pavlov repeatedly stressed that higher nervous activity was not, by any means, a sum of conditioned reflexes, and was not restricted to such. It is a broader concept that includes very complex kinds of inborn, unconditioned reflexes (instincts) and integrated systems of conditioned reflexes in the form of dynamic stereotypes, conditioned switching, and reflex chains in which the effector end of one reflex is the initial afferent link of the next, and so on.

A combination of Ukhtomsky's dominant focus and Pavlov's conditioned reflex, discovered and introduced into science by these outstanding leaders of world physiology, can be considered the elementary functional unit of the central organization of behaviour.

The mechanism of the dominant focus ensures *active search* for ways and means of satisfying a living creature's needs at a given moment. The mechanism of the conditioned reflex makes the generalized search selective, purposeful, and adequate to the existing situation. The two form a complex dialectical unity. Features of the dominant focus and all its characteristic behavioural,

electrophysiological, neurochemical, and microstructural attributes, for instance, are clearly discernible in the initial stage of the generalization of a conditioned reflex, while we find signs of a 'specialized dominant' (the third stage in the forming of a dominant focus, in Ukhtomsky's terminology) in the phenomenon of a backward conditioned connexion.

In the learning process and activity of the individual brain the principles of the dominant focus and the conditioned reflex are comparable with mutability and selection in the evolution of the world of animate creatures. The two mechanisms (dominant focus and conditioned reflex) organically supplement each other, making behaviour active and, at the same time, adequate to objective reality. The point here, we would emphasize, is not simply one of analogy but of a pattern of self-development of animate nature that is so universal that it is revealed in both phylogenesis (adaptation of a species) and ontogenesis (the adaptive behaviour of the individual). That is why we cannot agree with Popper's proposal: 'It is this theory of actively preferred conjectures and their refutation by a kind of natural selection which we propose to put in the place of the theory of the conditioned reflex.'\* Today's science of higher nervous activity has dialectically *integrated* active stochastic search and selection in the ideas it has formulated of the patterns and physiological mechanisms of the dominant focus and conditioned reflex.

The problem of learning, i.e. individually acquired experience, is examined by the authors in various aspects. The papers contributed by Rusinov, Kruglikov, and Gassanov are devoted to the cellular synaptic and neurochemical foundations of learning and memory. Those by Shevelev, Shuleikina, et al., discuss questions of the sensory system of adaptive behaviour. Livanov and Efremova explore the functional interaction of various cerebral structures in the forming of a conditioned reflex, by analysing the spatial organization of neural processes. Finally, the reflex, neurophysiological approach to the motivation of behaviour and the role of stimulation and reinforcing factors is reflected in the papers of Asratyan, Pavlygina, and Simonov.

In conclusion we would like to pay tribute to the memory of Esras Asratyan, the initiator, compiler, and executive editor of this volume. A pupil of Pavlov's and a worthy continuer of his work, E. A. Asratyan was the founder, and for many years director, of the Institute of Higher Nervous Activity and Neurophysiology (USSR Academy of Sciences). Throughout those years he was guided by the idea of constructive development of Pavlov's work

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\* K. Popper and J. Eccles. *The Self and Its Brain* (Springer International), Hamburg-New York, p. 138.

by integrating the latest achievements of the general physiology of the brain and the advances of allied fields of science, viz. neurochemistry, electron microscopy, radioelectronics, and computers. He developed ideas of the two-way (forward and backward or feedback) conditioned connexion as a universal principle of the brain's integrative activity, and suggested a reflex approach to understanding of the mechanisms of purposeful, motivated behaviour. Publication of this volume was one of his last scholarly undertakings. It embodies this remarkable man's enthusiasm and passionate search for truth.

*P. V. Simonov.*

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# The Polarization Electrotonic Hypothesis of the Formation of Simple Forms of Temporary Connexion

*V. S. Rusinov, Mem. USSR Acad. Med. Sc.*

For a perspective on the polarization electrotonic hypothesis one should consider the examples of simple forms of temporary connexion—summation reflex and the dominant focus, generally called the dominant. Though akin to the conditioned reflex in character, both differ from it by a number of significant attributes. In eliciting conditioned reflexes the summation reflex and the dominant are the initial phases of their initiation. So the latter two forms must be logically defined as temporary connexions or the initial phases of a single complex process leading to the rise of new connexions.

The dominant and its physiological mechanisms are more complex than the summation reflex. For one thing, the latter has not the large inertia that the dominant has. For another, if there is any conjugate inhibition during the summation reflex it occurs not in the way it does under the dominant. In that event, furthermore, conjugate inhibition differs from the conventional reciprocal reaction of inhibition because it exerts itself via the connexions brought about by newly formed interrelations in the central nervous system, and not via the connexions anatomically consolidated through the process of evolution.

The conditions for and phases of conditioning are well-known from the doctrine of higher nervous activity. The physiological mechanisms for conditioned reflex elaboration are genetically linked with summation. This is not to say that conditioned reflex is equivalent to either the dominant or summation reflex, even though both of them, by virtue of their mechanism, do have a role in the formation of a complex form of temporary connexion.

The general circuit diagram of the relation between the physiological mechanisms of summation reflex, the dominant and conditioned reflex may be dissimilar to the relation between specific forms of expression of the dominant and conditioned reflexes. This is because each of them can have a varied degree of complexity in terms of the structures involved in the reaction, levels of these structures and their implications for animal behaviour.

For our hypothesis, the starting theoretical assumptions have been the Pavlov theory for dynamic localization of functions and

the Ukhtomsky concept of the dominant. In the general context of his theory regarding dynamic localization of functions Pavlov introduced the concept of 'centre' as a functional integration of neural formations located on different levels in the central nervous system. Variable functions of the nerve cells in the cerebral cortex, according to Pavlov, depend on their *state* which, other conditions being equal, controls their response to a stimulus. Ukhtomsky, reasoning from Wedensky's teaching but drawing on other specific evidence, developed the same understanding of 'centre'. By general inference from Wedensky's teaching he accepted the proposition that the *functional state* of an excitable substrate, other conditions being equal, determines the reaction to a stimulus.

These general postulates by the classics of physiology premised our initial theoretical position for experiments with action by direct current on the cortex and subcortical formations. This was our line of reasoning: if indeed Pavlov and Wedensky with Ukhtomsky were right in assuming that the functional state of a neural substrate, other conditions being equal, does determine the response to a stimulus, then direct current must of necessity be made part of the experiment, much more on the cerebral cortex. The general physiology of the nervous system knows of no better factor to employ as the agent to modify gradually the state of a neural substrate than weak direct current. It was our feeling that by gradually modifying the intensity of direct current it would be possible to pick up all progressive alterations of the functional state and locate the optimum likely to give rise to the **exact state, necessary** for the formation of however simple, but still new, temporary connexion in the cerebral cortex.

The thesis suggesting for the state of a neural substrate a decisive role in determining, other conditions being equal, the reaction to a stimulus lays a bridge that joins the Pavlov doctrine with that of Wedensky-Ukhtomsky, its derivation from different experimental data notwithstanding.

The first fundamental principle of the polarization electrotonic hypothesis is this: *weak direct current, more precisely the electric field it generates, acts on the cerebral cortex modifying the state of the nerve cells there and is an essential determinant factor of change in the function of these cells.*

Based on pertinent experimental findings in our laboratory and data from the literature we have come to the conclusion (Rusinov, 1951) that overall rhythms of the electrical activity of the cerebral cortex suggest, first and foremost, the presence of a connexion between neurons that may have three different forms, or types, of expression. The first type of the functional connexion between neurons is a gradually spreading excitation (which we called 'local spreading excitation'). The second type is a propagating wave of excitation



shown electrographically as an action current, or action potential (AP). The third connexion type is electrotonic, that is, similar to the action of a direct current. All the three types of the connexion between neurons comprise a total connexion system, and thereby define the functional unity of the nervous system.

Let us examine these types of the functional communication between neurons to see which is the major one in the formation of simple forms of temporary connexion.

On present neurophysiological evidence, discrete processes in the nervous system—in the form of action potentials driving impulse transmission—occur mainly in the nerve fibre and not at the neuronal input and output, the critical integration sites of the neuron; the gradual processes in action there may be described as continuous functions. Some evidence in the literature suggests that changes in the state of the neuron may not necessarily be accompanied by the generation of an impulse but still influence the activity of neighbouring neurons, thus compelling recognition for the probabilistic character of neuronal discharge. There is no question that an electric field has the ability to modify the activity of neighbouring neurons. In other words, the processes going on in the nervous system make up a complex plexus of both analog and discrete properties of the system which is at once deterministic and probabilistic in character.

Much attention is being paid today to the functional role of gradual electrotonic potentials and their presumed involvement in information transmission to the neighbouring neuron, particularly, through dendrodendritic or axoaxonal junctions or even as a gradual process propagating via the axon itself.

In view of the methodological difficulties involved, there are as yet no accurate direct electrophysiological data on that score. There are nonetheless indirect pointers to possible conveyance of gradual electrical activity through the axon in the form of a monophasic potential. The proposition about the first type of connexion between neurons ensued from experiments with repeated KCl alteration of the sciatic nerve in the frog. Wedensky considered such a nerve segment and the processes set in train there in response to stimulation as an analog, a model of the cell in the central nervous system. Our laboratory offered a clear demonstration that under certain conditions, specifically after repeated alteration with KCl of a frog sciatic nerve segment, gradual potentials are able to radiate through the nerve in monophasic waves. Because of its resemblance with local excitation it was called 'local spreading excitation' but in fact this is gradual spreading excitation (Grindel and Rusinov, 1957).

Therefore, the concept of gradual spreading excitation as a possible type of functional connexion between neurons leaned on the

support of factual data. Frolov and Manyanin from the neurocybernetics laboratory of the Institute of Higher Nervous Activity and Neurophysiology have presently shown, using a mathematical model, that apparently an intermediate potential between the AP and electrotonic potential might propagate in dendrites of the central nervous system (CNS). Our first type of functional connexion between neurons is exactly the intermediate type between AP and electronic transmission. As is known, evidence for the possible transmission in the form of a gradual potential has been found also for the retina.

The American investigators Schmitt, Dev and Smith (1976) emphasize in the article 'Electrotonic Processing of Information by Brain Cells' that investigations of the latter day anticipate recognition of an important role for local circuits in higher brain functions (Schmitt et al., 1976). Among other things, they point to a major rethinking on the concept that information transfer between neurons requires the spike to spread. The data of the recent years indicate that minor gradual changes in one neuron may affect the electrical activity of other neurons (Dowling, 1970; Ezrokhi, 1970; Shepherd, 1974).

Our proposition for the third type of functional connexion between neurons was rested on the data of Wedensky and other scientists about the effect and long-distance effect in the nervous system of a weak direct current, meaning the physiological electrotonic. For, consistent with the Wedensky concept, we do distinguish between physical and physiological electrotonic. While the former is observable on live and dead nerves the latter is on the live nerve only. Consequently, speaking about the third type of functional connexion between neurons we mean properly the electrotonic effect similar to the effect of a weak direct current. Now it is common knowledge that the effect of a weak direct current on CNS can modify the distribution of interspike intervals. The study of the influence of a weak direct current (from 0 to  $10 \cdot 10^{-6}$  A) on cortical and subcortical formations was the central line of research in a series of our works devoted to the polarization dominant.

The second fundamental principle of the polarization electrotonic hypothesis for the formation of simple forms of temporary connexions reads as follows: *in addition to the presence and action of chemical and electric local fields, there exist three types of the functional connexion between neurons expressed bioelectrically as a spreading gradual potential, a well-familiar action potential, and an electrotonic interaction.* All the three types support the system of communication between neurons and participate in the formation of the dominant and initiation of the dominant focus.

It would be wrong to conceive of the dominant focus as a conglomerate of nerve cells located somewhere in the CNS as a grey

matter nucleus. We speak of the dominant focus having in mind the Ukhtomsky constellation, formed as a system during the organism's activity on all CNS levels in its different parts but with the primary focus of excitation in one part and with variable functions of individual components in the constellation. The dominant is but one of the stages in the functional evolution of an excitatory focus in the CNS. Not all excitatory foci can become dominant but only that which sets stationary excitation to a certain level fostering summation of the incoming excitations into the nervous system and tuning it to the optimal working rhythm for a given set of conditions, when an external stimulus, whatever its modality and site of excitation, is responded chiefly by that focus, while all other active foci are inhibited.

In our laboratory we sought a perspective on the nature of long-lasting electric potentials and the likelihood of the interaction between neurons through the medium of the extracellular field they set up, from a study on nerve cells of isolated crustacean receptors. The study has revealed that the action of non-specific altering agents transforms rhythmic background activity APs into group discharges and prolonged APs, the continuing exposure to these substances causes progressive depolarization of the membrane (Ezrokhi, 1967). The rhythmic discharges, prolonged APs and stable depolarization constitute the common reaction of neurons and their axons to the non-specific altering agents. Most authors explain prolonged depolarizing potentials, particularly those obtained in the cerebral cortex, in terms of summation of the excitatory postsynaptic potentials, while some attribute them to the intrinsic properties of the cell membrane itself. But because the nerve cells of the crustacean stretch receptors have no excitatory synapses, then apparently the receptor neuron reaction is due basically to modified membrane properties of the neuron itself.

Thus, long-lasting depolarization of cortical neurons can be conditioned not by postsynaptic potentials alone, for *stable depolarization, which is an electrographic way of expression for stationary excitation, can also be attributed to modified membrane properties of the neurons involved*. Put into a thesis form, this makes the third fundamental principle of the polarization electrotonic hypothesis for the formation of simple forms of temporary connexion.

In what way does a neuron in the state of stable depolarization affect its neighbouring neuron? Studies have found that the reaction of the neighbouring neuron to these influences is dictated by its state: whether it is in an active state and generates rhythmic discharges or it is inactive. It turns out that stable depolarization of one neuron releases a significantly greater frequency of discharges from its neighbouring neuron (Ezrokhi, 1970). The crustacean receptors lack the bridge between neurons in the form of a morpho-

logical substrate; therefore, the most probable cause of influence by the neurons' activity upon each other lies in the electric field originated during high-amplitude depolarization of either neuron's membrane.

It is worth stressing the low-threshold sensitivity, or high excitability of the neuron discharging spontaneous rhythmical AP to the voltage gradient building up in the ambient solution. The quantitative estimate of sensitivity of the crustacean stretch receptor neuron to the voltage gradient is cited by a number of authors (Terzuolo and Bullock, 1956; Ezrokhi, 1970). Excitability of the CNS neurons, judged by the index of their AP rhythm, varying with the effect of the external field, appears from the data in the literature to be even higher than that of the crustacean stretch receptor neurons, more so if the density of neurons in the cerebral cortex is considered. Thus, stable long-lasting depolarization may stem from changes in the membrane properties of neurons themselves, but, in addition, the increased activity of another neuron in response to stable depolarization of its neighbour suggests possible involvement in functional connexion between neurons of the extracellular electric field produced by the nerve cells themselves.

Electrogenic membranes become increasingly a frontier area of research in contemporary neurophysiology. Until recently, the primary focus has been on the generation and conduction of neural impulses displayed electrographically in the AP form. But then the problem of neural impulse is only a part of the more general problem, that of the functional connexion between neurons which is not achieved and maintained by impulses alone. So today's research on excitable membranes is characterized by a shift of emphasis toward the molecular level, a striving to gain insights into the molecular nature of the membrane processes, an inquiry into the transport of ions through membranes, an analysis of ionic channels, their composition and structure; and—our special curiosity here—the dependence of conductivity of the ionic channels on a weak electric field. The latter is of special interest in the context of the polarization electrotonic hypothesis because the rise of a simple temporary connexion under the dominant is likewise contingent upon variation of the weak electric field.

It has been made clear in the literature that an excitable membrane presents a non-linear ionic conductor which depends for a good deal of its properties on the electric field. The existence of two distinct conduction systems, sodium and potassium, has been proved and the role of the sodium and calcium channels in generating trans-membrane input currents has been elucidated with a new set of methods (Kostyuk et al., 1976).

Lately, a new class of substances has been discovered, called ionophors, which can alter dramatically the electrical properties

of membranes. In their presence membrane conductivity shoots several orders upwards (Markin and Chizmadzhiev, 1974; Ovchinnikov et al., 1974). Ionophors themselves are needed in minor quantities. Their only involvement is to transfer other ions across the membrane, this conductivity being selective. The chemical substances dissolved in the intercellular fluid may be influenced by the electric field so as to take on the role of ionophors. The conducting structures of biomembranes operate essentially as channels and, in the general estimate, there are hundreds of Na channels per one  $\mu\text{m}^2$ . The nature of the ionic channels is perceived in a number of ways. Some authors contend that ionic channels are not pre-existent in biological membranes so the increasing conductivity with depolarization has to do with their assembly. A wider accepted notion says that the channels are pre-existent and represent a macromolecular system with an ability for conformational readjustments. Examination of the conductivity of channels as a function of the electric field leads one to believe in their restructuring once there is a change in the external electric field. This runs parallel to alteration of their ionic permeability as caused by a variety of reasons that are not clearly understood at present. Some of the probable causes include conformational changes in the system of channels, their 'opening' or 'closing', and a reorganization of the channels' molecular geometry.

Facts bearing directly on the formation of the dominant focus cannot be attributed solely to the changes taking place in the neuronal membrane. The effect of anodic polarization is not confined to the local alteration of the membrane potential, it affects immediately also other structures of the cortex and subcortical formations. The focus of excitation in the cortex, set up by direct current, possesses certain histological and histochemical characteristics. The shift occurs not in the pyramidal cells alone, but also in the interneurons and glial cells (Brazovskaya and Pavlygina, 1972). Different cortex elements respond as a single functionally organized ensemble, or a system. The incorporation of various elements into the system is differentiated with respect to time.

The expression of a long-lasting trace effect following cortex polarization cannot be related to the alteration of the membrane potential, known to return practically at once to the initial level once the direct current is switched off.

What is then the type of connexion or signalization between neurons that is meaningful and essential for the connecting function and the formation of temporary neural connexion? This is the hypothesis we have found sufficiently justified to merit acceptance: the type of connexion between neurons in the form of electrotonic influences is the most essential one for the formation of temporary

connexion (Rusinov, 1953a; Rusinov, 1953b). As a corollary, the extracellular field bringing electrotonic influences to bear on the system of neurons can actively establish and sustain the optimal state of two separate cortical points and, presumably, initiate a unified adequate response to the stimulation, enabling an indifferent stimulus for a particular activity to become a signal one and replace an unconditioned stimulus.

The type of connexion in the form of an electrotonic influence is the one most similar in character to the action of direct current. Consequently, if a direct current applied through a point electrode placed at the forelimb representation point of the rabbit cortex fails to produce by itself any effect on the periphery but changes exclusively the state of the given cortical site (the second, reference electrode is located on the nasal bone or ear) then, if the hypothesis is true, an 'interconnection' should come up between the two excitation foci and the forelimb would contract in response to light, for example.

The experiments to validate the hypothesis were first reported at the 19th International Congress of Physiologists (Rusinov, 1953a) and then amply confirmed in the series of studies accomplished in our and other laboratories. Their detailed discussion is in the monograph (Rusinov, 1973). For now we shall abstract for discussion only the data most immediately bearing on the problem in question—the polarizational electrotonic hypothesis for the formation of simple forms of temporary neural connexion.

To produce a dominant focus in the cerebral cortex, an anode of weak direct current was employed. Why the direct-current anode? Let us review in brief the effect of the direct-current anode on the nervous system. The well-known Pflueger's law regarding the action of direct current and the excitation said to come from the cathode holds true only for peripheral nerves and moreover in their normal, and not altered state. Ever since the times of Sechenov (1882) it has been known that for the medulla oblongata exposed to a direct current excitation originates from the anode. One is likewise familiar from the literature with the experience of Fritsch and Hitzig (1870) who were the first to stimulate the motor cortex in man but who could obtain a motor effect only on stimulation with the direct current anode. Vinogradov (1914-1915) was the first to show that the function of conductivity in an altered nerve segment that had once lost it, could be re-established by exposure to the anode of a weak direct current. This restorative anode effect was subsequently detailed by a number of researchers (Rusinov, 1934; Narahashi, 1964; Vasiliev, 1924). If there is not one but several altered parts in the way of an impulse run in the nerve it is sufficient under these conditions to act with the anode upon the first of the parts along the impulse run to reinstate conductivity

in the whole nerve. It is sufficient, moreover, to apply the anode of a weak direct current of optimum intensity to the topmost portion of the first part or even only its input in order to obtain a fully restored conductivity in the entire nerve (Rusinov, 1930). If, in agreement with Wedensky, one considers the altered nerve length to be a model of the nerve cell then the working hypothesis to arrive at, by way of logical inference, is that the weak direct current anode of optimal intensity rebuilds cell conductivity through its action on both, the presynaptic and postsynaptic neuron input.

A study of the ultrastructure of axosomatic and axodendritic synapses of the motor cortex of a rabbit has put together the notion of the polarization dominant as a near-physiological phenomenon, whereas the changes thus identified in the ultrastructure of the synapses fit into the mold of functional alterations. Analytical treatment of the results obtained showed a statistically significant increase in the number of the synapses with a large quantity of synaptic vesicles in the lower layers of the motor cortex. The data reveal increasing functional activity of the synapses in the dominant focus (Artyukhina and Ryabinina, 1972). Further electron-microscopic investigation made it clear that the increasing functional activity of the synapses was accompanied by changes in both, the presynaptic and postsynaptic, components of the axodendritic synapses; it is in the postsynaptic matrix, however, that the reaction was most in evidence under the motor dominant. Here, moreover, some difference began to take shape between the simple reaction of summation and the dominant. In the latter instance the 'thickening' of the postsynaptic membranes was more pronounced.

These changes will be reviewed below in the light of the electrophysiological data available in the literature and those obtained in our laboratory, in terms of the polarization electrotonic hypothesis for the formation of simple temporary connexions.

A direct current in the initiation of the polarization dominant affects primarily, if only dissimilarly, all the elements of the motor cortex within the borders of the electric field produced by it. This effect becomes apparent as a change of the animal's functional state and ultrastructural variations suggestive of an increase in synaptic activity. What kind of synaptic activity are we talking about? It is the activity of the synapses driving chemical transmission of neural impulses. Yet we are now aware of the so-called electric synapses to be found both in lower vertebrates, and in the invertebrates as well. In the electrical synapses there is no chemical transmitter secretion. Besides sites have been discovered in the cerebral cortex, in which dendrites with dendrites might conduct. It was previously held that dendrites never appeared in the capacity of a presynaptic component. The classical conception of one-way conduction in the central neuron with regard to the dendrite

as only a receptor structure needs to be updated now. For the dendrite has been shown to be not merely the receptor structure upon which postsynaptic components are organized, it may be also a presynapse transforming information to other neurons through dendrodendritic synapses. In particular, dendrite-formed pre- and postsynaptic components were detected in the olfactory bulb (Rall et al., 1966). So far this type of dendrodendritic synapses have been found only in the olfactory system but there is no denying their likely existence, as also of electric synapses, in other CNS regions, the cerebral cortex among them. The polarizational electrotonic hypothesis suggests their presence mainly in the upper cortical layer, the assumption prompted by the following considerations.

The lower layers of the cortex seem to be more important not at the moment of effective communication via a temporary connexion, but when traces are in the making and the already elaborated connexion is to be sustained. As the surface of the motor cortex in the rabbit is stimulated by pulsating current at a certain rhythm, the rabbit responds to uninterrupted light or sound stimulation with the proper limb movements at the rhythm equal to the current pulsation. When the rhythm of the pulsating current has been modified in the same experiment, the upper cortical layers, so far as can be judged by the proper EEG and the data of its frequency analysis, assimilate the new rhythm, yet the rabbit responds to the uninterrupted stimulus with limb movements at the previous, and not the new rhythm (Pavlygina and Pozdnyakova, 1960). These findings indicate that the deeper-lying cortical structures maintain longer the old rhythm (and at that very rhythm the impulsation reaches the effector) than do the structures that experience the immediate effect of direct current at a given moment, from which the EEG is being recorded.

The form of the electric field in the rabbit cortex was then studied using the methodology accepted in our laboratory for the initiation of the polarization dominant. It transpired that with a superficial polarization across the pia mater the field was flattened and the isopotential lines extended along the surface of the cortex (Egorov and Kuznetsova, 1972). The effect was apparently as much a result of the current spread over the cortical surface through the fluid film, as it was also of the complicated geometry of the brain cortex and unequivalent conductivity of the latter's structures. The potential gradient was maximal in the superficial layers but below them the potential decrement was more smooth. Thus the study of the form of the electric field under the polarization dominant has shown that the area of the maximal potential gradient coincides with the first cortical layer. Hence it follows also, as a logical conclusion from the polarization electrotonic hypothesis, that the upper cortical layer is the most likely locus for the existence of electric



synapses varying their function under the simple form of temporary connexion, more particularly the latter's model in the form of the polarization dominant.

Interestingly, contacts of the electric synapse type present actually as an astrocyte-dendrite membrane junction, i.e. glio-dendritic synapses, were discovered by Artyukhina and Ryabinina who studied ultrastructural changes in the upper cortical layers of the rabbit brain under the polarization motor dominant. The same study discovered desmosome-like, glio-dendritic and dendro-dendritic contacts.

These phenomena have been found out using superficial cortex polarization with a weak direct current that evokes the dominant. Now one can understand the difference seen by some authors between polarization of the rabbit motor cortex surface and single cortical neurons, when the superficial polarization has been the more effective. These data, along with some other, testify to the functional importance of an electric field in producing the simple form of temporary connexion.

As a working hypothesis supported by some known facts, it is possible to state the following: *in cortex polarization with direct current and the rise of the polarization dominant as an alternate simple form of temporary connexion the lower cortical layers become a scene of essentially biochemical shifts in chemical synapses, the upper layers a scene of changes primarily in electric synapses and the entire cortical mass a scene of alterations in the ionic mechanisms of the electrogenic membranes.*

The polarization electrotonic hypothesis treats the polarization-induced changes on cell membranes only as a primary stage in the mechanism for the formation of the simple forms of temporary connexion. After that organization of the dominant system begins to engage the structural and biochemical shifts triggered in the cortical structural elements by long-lasting electrotonic influences.

The fourth fundamental principle of the polarization electrotonic hypothesis reads: *the electrotonic type of interaction in cortical neurons influences is key determinant in the formation of simple forms of temporary connexion.*

In the literature it is usual to distinguish between electrotonic influences which demand an appropriate structure for their transfer and the influence of electric field. This question requires special treatment. For the moment it is worth stressing that both influences are gradual non-impulse types of CNS influences classified with non-linear processes. Clearly, the functional electrotonic is a case in point, with its influence over some distance and perhaps even with a long-distance effect in the CNS.

The facts covered in the previous sections favour the polarization electrotonic hypothesis because they are more easy to explain

by reference to the mechanisms of the electrotonic interactions similar to the action of direct current, because some of them relate to extrasynaptic influences, and because the influences of electric field fall into their category.

What is it, then, that in the natural conditions of animal life, and not in laboratory experiments, plays the role similar to the cortex polarization with a direct current, the role of the 'initiator' of the dominant focus? To that question the literature replies in a number of ways. Ukhtomsky singled out a gradually subsiding electrical skin stimulus for being especially favourable to the initiation of the focus in the motor cortex, the concept reconfirmed in our laboratory (Ukhtomsky, 1950; Grechushnikova, 1962). Humoral factors may well provide the organizing force for the dominant focus (Uflyand, 1925). One may concede the validity of Rabinovich's proposition for the importance of polysensory neurons in the 'trace-coupling' mechanism in conditioning. Of particular interest in this regard is the rise of a depolarization analogous to the dominant focus, brought about by long-lasting proprioceptive stimulations (Voronin, 1966; Rabinovich, 1975). Overall these findings give legitimacy to the idea of dominant foci of the polarization electrotonic character arising in natural conditions.

Of the late years, a large number of studies have been collected in the literature indicative of slow gradual potentials present not only in animal but human CNS as well. Thus the essential role of the electrotonic processes for brain functions is established further. And, while a review of these studies is beyond us in the present paper, the fact itself gives credibility to possible emergence in nature of such gradual electrotonic potentials, which mirror the lengthy processes fostering the initiation and maintenance of dominant foci.

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# 2

## Some Neurochemical Correlates of Learning and Memory

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Current conceptions on the neurochemical support of learning and memory processes assign a key role there to diverse kinds of neuromediator effects and the allied metabolic changes in nucleic acid and protein macromolecules, and also to neuropeptides. Greater in-depth understanding of the neurochemical bases of learning and memory calls for specifying the role and clarifying the participation mechanisms of the factors just mentioned in the integrative activity of the brain.

This general concept provides an initial theoretical assumption in researches by scientists at the laboratory of neurochemical mechanisms of conditioned reflex. The major methodological principle of the research, physiologo-biochemical correlations, translates into studies focusing on two types of influences—those that learning and memory processes have upon cerebral metabolism and those that guided interventions into cerebral metabolism have on learning and memory processes. It is through the use of these and some other, less general, approaches that factual data have come to hand taking one step further towards refining and updating the present ideas about the neurochemical mechanisms of learning and memory.

To appreciate the role of cholinergic and cholinoreactive cerebral mechanisms in these processes the widely used method is estimation of acetylcholinesterase (AChE) activity in cerebral structures at different stages in the development and maintenance of conditioned reflexes. Another line of research dealt with is how these processes are influenced by the blockade of cholinoreceptors. The studies completed to date have suggested that the formation and subsequent consolidation of conditioned reflexes cause lawful changes of AChE activity in the sensomotor and visual cortex and hippocampus. The thrust and extent of these changes depend on the type of the reflexes being formed, their degree of stability and the time span between the termination of functional load and the investigation of AChE activity (Table 2.1).

If analysed, the tabulated data reveal a number of essential points. When a defensive conditioned reflex has barely been elaborated, the AChE activity of the sensomotor cortex and hippocampus

**Table 2.1.** Activity of Acetylcholinesterase (AChE) in Rat Brain in the Development and Consolidation of Defensive and Feeding Conditioned Reflexes (Experiment) and with Unpaired Presentations of Stimuli ('Active Control') in Percent to Passive Control

Group of Animals	Type of conditioned reflex	Sensomotor cortex		Visual cortex		Hippocampus	
		Exper.	Active control	Exper.	Active control	Exper.	Active control
Decapitation right after the 1st trial	defensive feeding	80.50*	145.75*	99.15	114.40	76.94	103.96
		144.57*	141.69*	129.46	164.45*	114.26	82.69
Decapitation in 24 hrs after the 1st trial	defensive feeding	118.41	107.91	102.75	68.50*	114.16	82.90
		68.62*	88.69	70.37	91.66	99.26	92.61
Decapitation right after the 20th trial	defensive feeding	82.20*	117.69	80.86	109.56	75.06*	78.76
		68.85*	84.42*	66.93*	80.00	75.59	88.18
Decapitation 24 hrs after the 20th trial	defensive feeding	108.07	99.03	102.75	93.80	87.35	67.34*
		69.94*	84.30*	74.95*	91.20	99.40	91.44

\*  $P < 0.05$ .

decreases. Conversely, immediately upon the conditioning of a feeding reflex AChE activity increases in the sensomotor and visual cortex, and the hippocampus. In the 24 hours after the reflexes were developed the thrust of the shifts changes to the opposite: the decreased AChE activity just after the conditioning of defensive reflexes will have grown by that time, and the increased activity immediately following the conditioning of feeding reflexes will have dropped.

AChE activity changes followed a somewhat different pattern after the stabilization of conditioned reflexes was accomplished in a series of 20 experiments. As seen from the data in Table 2.1, the AChE activity of the sensomotor and visual cortex and hippocampus declined shortly after the 20th experiment in the stabilization of the defensive conditioned reflex, only to shoot again 24 hours later. But, after the 20th experiment in the stabilization of feeding conditioned reflex AChE activity, as contrasted to what it had been just after the 1st experiment, decreased and remained low until 24 hours after experiment.

Unpaired stimuli presentations, as is clear from Table 2.1, also result in fairly pronounced changes of AChE activity. Furthermore, the unpaired presentations of light and electrical skin stimuli produce shifts for the major part opposite in direction to the shifts brought about by the development of the defensive conditioned re-

flex. The shifts of AChE activity in response to unpaired presentations of light and food stimuli are of a somewhat different character. In the initial experiment, AChE activity in the sensomotor and visual cortex of the animal group comprising the active control (AC) rises and the shift that occurs is of the same direction as in the development of conditioned reflex. One day after the initial experiment, as also immediately and one day after the 20th experiment, shifts of AChE activity in the cerebral structures of the AC group animals appear to be essentially identical in character to those observed in the conditioning of the motor-feeding reflex.

One of the probable causes for these differences is that in the defensive situation elaboration of the escape or avoidance conditioned reaction terminates or prevents the painful stimulation if certain motor reactions have been carried out. In the case of unpaired stimuli presentation, however, the animals experience painful stimulation, whether or not the light is on or particular responses have been made.

In the feeding situation somewhat different relations are obtained, as required by the experimental procedure: the animals obtain food both during conditioning and on being presented with unpaired stimuli. In the assessment of the dynamics of AChE activity shifts in animals to whom both light and electrical skin stimulations were presented without pairing, one must bear in mind a whole range of relevant factors including the extinction of the orientation reflex and development of the defensive reflex to the situation.

The fact that the AChE activity changes in the cerebral structures have been observed, in particular, after the 20th experiment in the stabilization of the defensive conditioned reflex leads to thinking of these changes as being conditioned in nature. The reason for the supposition comes from the stability with which the avoidance reflex to light was displayed by the test animals by the 20th experiment, though they had no electrical skin stimuli applied in the first few experiments.

A special series of experiments failed to detect any difference in terms of AChE activity in the sensomotor and motor cortex and hippocampus one month after the conditioning of a defensive reflex between the test animals and the control exposed to the action of unpaired stimuli. One could thus assume that the conditioned reflexes persisted not because of the retained AChE activity changes after their development, but because of the reactivity changes in the cholinergic cerebral mechanisms relative to the signal (conditioned) stimuli.

To check the assumption steps were taken to form the defensive conditioned reflex in the test animals; meanwhile the animals

in the AC group were presented with an appropriate amount of unpaired light and electrical skin stimulations. Then the AChE activities of the cerebral structures were estimated one month post-training, and the retention of the reflexes was verified in some of the test animals before decapitation by relearning them. The corresponding AC animals were presented with light and electrical skin stimuli out of pairs. The results of the experiments are summarized in Table 2.2.

**Table 2.2.** AChE Activity of Sensomotor and Visual Cortex and Hippocampus in Trained Rats and Active Control (per  $\mu\text{M}$  of hydrolysed acetylcholine (1 mg protein/min))

Variant	Animal group	Sensomotor cortex	Visual cortex	Hippocampus
No light and electro-skin stimuli presented	Active control	$0.589 \pm 0.150$	$0.560 \pm 0.122$	$3.502 \pm 0.578$
	Experiment	$0.560 \pm 0.147$	$0.471 \pm 0.041$	$2.927 \pm 0.354$
Light and electro-skin stimuli presented	Active control	$0.537 \pm 0.110$	$0.550 \pm 0.138$	$2.852 \pm 0.530$
	Experiment	$0.251 \pm 0.037^*$	$0.268 \pm 0.045^*$	$2.106 \pm 0.419$

\*  $P < 0.05$  as compared with active control.

As shown in Table 2.2, the relearning of conditioned reflexes in trained animals induces a dramatic lowering of AChE activity in the sensomotor and visual cortex, whereas in the AC animals repeated presentations of unpaired stimuli left AChE activity unaltered. This supports the view that reflex conditioning does alter the reactivity of the cholinergic brain mechanisms. The altered (increased) reactivity is retained after the conditioning and provides one of the mechanisms sustaining the corresponding engram (temporary connexion). This conclusion is in line with the well-known hypothesis by Deutsch (1974). It has prompted amongst other things, an experimental series concerned with assessment of variations of ACh sensitivity in the neurons of the sensomotor cortex in the rabbit in defensive reflex (to sound) conditioning and extinction.

A study carried out by this author in collaboration with Koshoyantz and Valtsev showed the neurons in the sensomotor cortex of a rabbit to become high ACh-sensitive once they become involved in the production of temporary connexion. The neurons' responses to micro-ionophoretic ACh application is lawfully potentiated to be well above the initial ACh responses of these neurons and of those neurons which do not change their activity despite stimulus pairs presented to them (Fig. 2.1). This evidence, along

with the earlier obtained data by Schmidt et al. (1974), confirms the assumption for changes in the chemoreactive properties of neuronal membranes, particularly their increasing ACh sensitivity, to be the basic cause for the formation of temporary connexion (engram). Additional support for the same assumption comes from the observed reduction in ACh sensitivity of most neurons in conditioned reflex extinction. Though most neurons decrease their ACh sensitivity (Fig. 2.1, *C*) some of the neurons do not—rather they

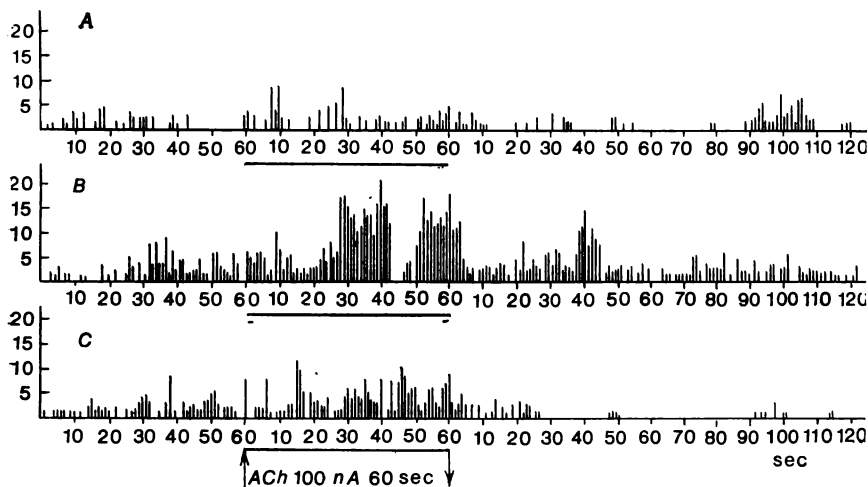


Fig. 2.1. Changes in responses of sensomotor cortex neurons to microionophoretic application of acetylcholine (ACh).

*A*—ACh response prior to reflex conditioning; *B*—same, after the conditioning; *C*—same, after extinction of the conditioned reflex.

maintain the previous above-normal level or even push it up further (Fig. 2.2). It is most likely that the neurons with steadily increasing ACh sensitivity are those most immediately related to the maintenance of temporary connexion by virtue of being the latter's constituents. One essential aspect concerns the less pronounced character, overall, of the changes in the reactions of cortical neurons to microionophoretic glutamate application during the formation and extinction of the conditioned reflex. Largely, the changes were confined to the structure rather than the intensity of those reactions, as can be seen from Fig. 2.3.

One cannot help noticing, in particular, the rise of an after-effect, following the end of the glutamate application, in the neurons that have changed their activity (Fig. 2.3, *B*). The fact is the more noteworthy because the absence of any after-effect, that is, the re-establishment of the initial activity right after the microionophoretic



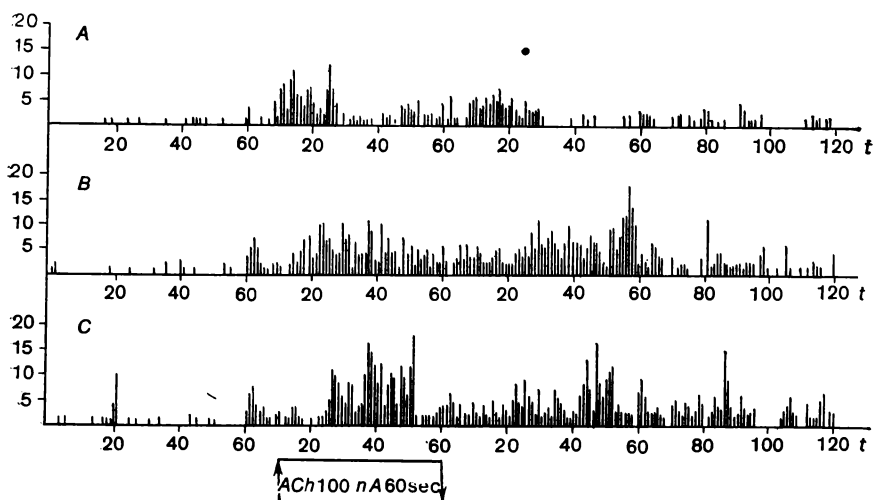


Fig. 2.2. Potentiation of responses by sensomotor cortex neurons to microionophoretic application of acetylcholine (ACh) after extinction of conditioned reflex. Symbols are the same as in Fig. 2.1.

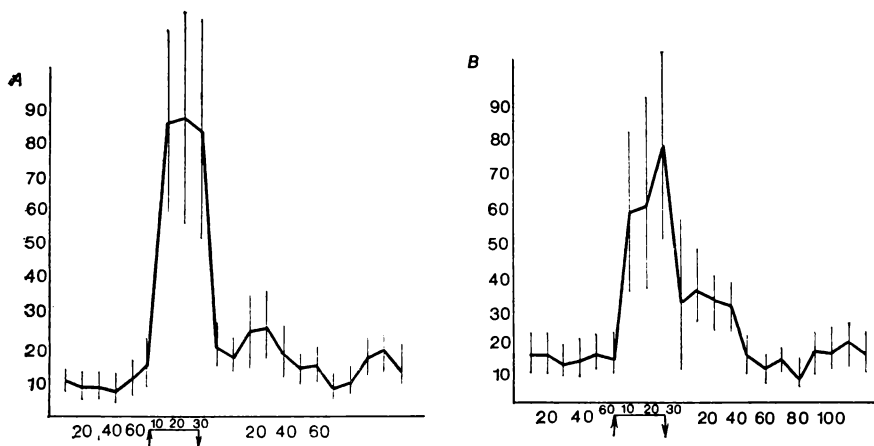


Fig. 2.3. Averaged responses of sensomotor cortex neurons to microionophoretic application of L-glutamate before (A) and after (B) conditioning.

The ordinate is the number of impulses during 10 sec; the abscissa is time in sec.

application of the amino acid is halted (Fig. 2.3, A), is an extremely common characteristic of glutamate in the norm. There is a high probability that postconditioning readjustments in the chemoreactive properties of the 'trained' neurons' membranes also contribute to the changes in the reactions to glutamate.

Another line of research designed to shed light on the specific involvement of the cholinergic brain mechanisms in learning and memory processes explored the influence of the blockade of ACh receptors upon the processes. In the course of this research, the blockade of the ACh receptors by benactizine or scopolamine was found to produce only moderate disturbances in the learning process, but to grossly violate the fixation of temporary connexions, causing amnesia. The kind of amnesia brought about in mice by 2.5 mg/kg of scopolamine is easy to eliminate with a 'reminder'. Yet the increase of the scopolamine dose to 5 mg/kg renders the 'reminder' totally ineffective, suggesting that perhaps the blockade of the ACh receptors holds down the effectiveness of the consolidation process until it is fully suppressed. In sum, the above data lead one to conclude the participation of both cholinergic and cholinreactive cerebral mechanisms in the development of temporary connexions and their fixation, too.

The ways in which monoaminergic brain systems become part of learning and memory processes were investigated by studying the influence of guided interventions of the systems' activity upon the elaboration and retention of temporary connexions. The studies completed, it became evident that pharmacological or surgical interventions in the activity of serotonergic and catecholaminergic cerebral mechanisms affect dissimilarly the formation and fixation of temporary connexions. To let serotonin (5-hydroxytryptamine, or 5-HT) build up in the brain, monoaminoxidase (MAO), a monoamine-splitting enzyme, had to be suppressed and iprazide had to be used for the purpose. After that, the serotonin excess was seen to produce a rather peculiar effect: the conditioned reflex of passive avoidance (CRPA) that had been elicited with excessive brain 5-HT in the background persisted in rats for a few dozen minutes whereafter deep and stable amnesia set in (Fig. 2.4). CRPA retention in the 15 minutes after the conditioning and the advent of stable amnesia one hour after the conditioning lend themselves to three important conclusions: (1) reflex conditioning with an excess brain 5-HT in the background is distinctly possible; (2) an excess 5-HT in the brain does not preclude the reproduction of the engram (temporary connexion); and (3) information storage mechanisms in the brain are relatively stable, at early phases, to excess 5-HT. It thus follows that the process of information transfer from short-term into long-term memory, or the process of consolidation, is the 'point of attack' for the excess brain 5-HT. This in-

ference found confirmation in 5-HT studies with a broad spectrum of conditioned reflexes with due regard to the parameter of age and individual characteristics of test animals.

One particular finding indicated an increasing 5-HT content in the hippocampus with ageing and its accompanying reduced efficiency of the consolidation process. A related finding indicated that the variation of 5-HT content in the brain of old animals with reflex conditioning has a different character than in young animals. These data were obtained by the authors, Getzova and Unial, from

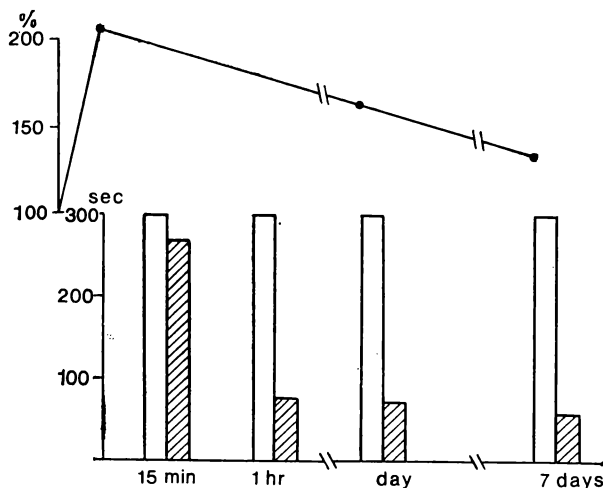


Fig. 2.4. Dynamics of retention of CRPA elaborated against the background of excessive serotonin in the brain. Unhatched columns denote control and hatched ones denote experiment. The upper curve shows the dynamics of serotonin content in the brain.

a study on rats of two age groups: old, from 15 to 18 months; and young, aged 8-10 weeks. The 5-HT content was successively estimated in the brain of non-trained animals and also in animals right after and 7 days past the conditioning of the defensive reflex.

To equalize the reflex-conditioning settings for the young and old animals, both were presented in a Y-shaped maze with 50 combinations of light and electrical skin stimuli, and the number of correct responses—escapes and avoidances—were recorded.

As is clear from Table 2.3, the hippocampal 5-HT content of the old rats is significantly and reliably higher ( $P < 0.05$ ) than that of the young rats. For the other structures under investigation, that is, the hemispheres (minus hippocampus), diencephalon, midbrain and medulla, the old animals exhibited lower 5-HT content than the young ones. Conditioning influenced all the examined brain regions by depressing the serotonin content in the young animals



and, conversely, elevating it in the old. After seven days post-training the serotonin content in the brain of the young animals largely returns to normal, but in the older animals it still remains significantly and reliably above normal.

The result is an altogether different relation between the respective serotonin concentrations in the cerebral structures of the old and young animals right after and seven days post-training than it is in the brain of untrained animals, in whom the serotonin content in all structures is higher for the old than for the young animals. Following the conditioning of defensive reflex, the hippocampal serotonin content decreases by 34 per cent in the young animals and remains almost level in the old ones. The decrement of the serotonin content in the other structures is within 12 to 27 per cent for the young animals and its increment ranges from 43 to 53 per cent in the brain of the old animals.

This indicates that, in the old animals, training fails to reduce the hippocampal serotonin content as it does in the young animals, whereas in the other cerebral structures the shift in the old animals is twice that of the young ones.

It is generally known that the role presently ascribed to the hippocampus is as one of the primary links in the mechanism of information transfer from short-term to long-term memory. Our findings regarding the rise of the serotonin content in the hippocampus of the old animals, in whom the consolidation process has a reduced effectiveness, can lend additional support to the proposition that excessive serotonin has an adverse effect on consolidation. It should be pointed out, on the other hand, that conditioning in old animals is attended by an increase, and in young ones by a decrease in the brain serotonin content. It is probable that the initial excess of serotonin in the hippocampus and the increasing content of this monoamine in the other cerebral structures with conditioning predetermine the decreasing efficiency of the consolidation process in the old animals.

The apparent 'rigidity' of the shifts in serotonin concentrations in the brain of the old animals as affected by conditioning is also noteworthy. Table 2.3 illustrates that a week after the reflexes were conditioned the content of serotonin in cerebral hemispheres and the midbrain, diencephalon and medulla oblongata of the old animals remained elevated. By that time the serotonin content in the young individuals had returned to its initial values.

In a special series of experiments on young animals the retention indices of developed conditioned reflexes were compared against the 5-HT content in the cerebral structures involved. The comparisons revealed a confident inverse correlation of the 5-HT content in the hippocampus, midbrain and medulla oblongata with the retention index of conditioned reflex within 7-10 days post-condition-

ing. The data, even though they suggest some 5-HT involvement in the consolidation process, were nevertheless of an indirect character and clearly in need of direct experimental support. Such direct supporting evidence for the negative effect of excess 5-HT in the brain upon the consolidation process could derive from incidents of amnesia that develop in animals because of an excess of 5-HT immediately after, and not prior to, training.

Such data were gained by Essmann from intra-hippocampal 5-HT injections immediately following CRPA conditioning in mice. But, aware that even point lesions of the hippocampus after training are able by themselves to cause amnesia, we adopted another approach to increasing 5-HT content in the brain. This was by intravenous injection of 5-hydroxytryptophane (5-HTP), the 5-HT precursor, easily passing through the haematoencephalic barrier. It has thus been found that a 5-HTP injection before CRPA conditioning drastically impairs its retention capacity 24 hours later; 5-HTP injection right after CRPA conditioning also worsens retention but only slightly (insignificantly); and a 5-HTP injection one hour post-training has virtually no effect. The most probable cause for the lack of effect from the 5-HTP injection immediately after training lies in relatively delayed 5-HT buildup in the brain.

Consolidation is known to be maximum-sensitive to the effect of amnesia-causing agents in its very early stages. In the case of the 5-HTP injection immediately after training these stages will have run out even before 5-HT has time to synthesize in the brain from 5-HTP in 'sufficient' amounts. To test the assumption required the consolidation process to be slowed down somehow, so that its very early and most vulnerable stages be exposed to the effect of the 5-HT accumulation in the brain. Decrease of the brain temperature is generally recognized as being one of the ways to achieve artificial deceleration of the consolidation process.

With this in mind, in the experimental series that followed 5-HTP was injected in combination with cooling exposure of the test animals. Because of the necessity to slow down the very early consolidation stages, that came following the reflex conditioning within a brief interval, the animals' cooling had been completed prior to the conditioning. In the belief that the slowing-down rate of the consolidation stood in proportion to the extent of the animals' cooling exposure, the latter was employed in the experiments in two gradations, keeping the animals respectively at  $+5^{\circ}\text{C}$  and  $-7^{\circ}\text{C}$ . The next step after the cooling consisted of CRPA conditioning in the animals, followed by intravenous injection of 5-HTP or physiological solution. The results are presented in Table 2.4.

As distinct from the post-training 5-HTP injection in ordinary conditions, the 5-HTP injection after cooling and training leads to pronounced amnesia whose severity was the greater, the harsher

**Table 2.4.** Influence of Cooling Exposure and 5-HTP Injection at 100 mg/kg upon CRPA Retention in Mice

Group of animals <sup>1</sup>	Time of stay in 'safe' compartment, sec		P
	Initial experiment	Retention check-out 24 hrs later	
1. 5°C 30-min exposure, CRPA conditioning, injection of physiological solution ( $n=46$ )	38.80±3.78	300	< 0.05
2. 5°C 30-min exposure, CRPA conditioning, injection of 5-HTP ( $n=37$ )	43.20±4.15	200 (66.6) <sup>2</sup>	
3. -7°C 5-min exposure, CRPA conditioning, injection of physiological solution ( $n=28$ )	32.20±3.52	257	< 0.05
4. -7°C 5-min exposure, CRPA conditioning, injection of 5-HTP ( $n=26$ )	34.30±4.05	102 (39.7) <sup>2</sup>	
5. CRPA conditioning, injection of physiological solution, -7°C 5-min exposure ( $n=23$ )	31.20±5.02	300	> 0.05
6. CRPA conditioning, injection of 5-HTP, -7°C 5-min exposure ( $n=20$ )	38.20±3.73	245 (81.6) <sup>2</sup>	

<sup>1</sup>  $n$  = number of animals.<sup>2</sup> ratio to corresponding value in control, %.

the cooling exposure. To appreciate this principal result of the experiments it is essential to consider several important points. To begin with, there is the fact that the cooling exposure per se hinders neither CRPA elaboration nor its subsequent retention. Table 2.4 makes it clear that the time of stay in the 'safe' compartment of the apparatus for the animals unexposed to cooling prior to the CRPA conditioning (groups 5 and 6) and those exposed to pre-cooling was 31-38 and 32-43 seconds respectively. Since the time of stay in the 'safe' compartment of the apparatus in the initial experiment is commonly regarded as a characteristic of CRPA elaboration, it may be stated that, overall, the cooling exposure virtually did not affect the reflex conditioning. Nor did the cooling exposure, whether before or after training, affect the CRPA retention. The retention index for the corresponding groups of control animals, as suggested by Table 2.4, was 257-300 seconds, practically equivalent to the unexposed control animals.

However, while the cooling exposure applied singly failed to influence the CRPA retention, it did induce amnesia if used in combination with a 5-HTP injection. Moreover, the injection of one

and the same 5-HTP dose of 100 mg/kg caused more deep amnesia in the animals kept at  $-7^{\circ}\text{C}$  (their retention index being 39.7 per cent of control) than in those kept at  $+5^{\circ}\text{C}$  (their retention index being 66.6 per cent of control). The perceived relationship between the depth of amnesia in the animals versus their extent of cooling may be viewed as an argument in favour of the notion that it is cooling exposure, rather than any other factor, which has the most essential role in the causation of amnesia, along with the 5-HTP injection.

It is thus concluded that an excess 5-HT, when set up in the brain after training, interferes in a very real sense with the consolidation of temporary connexions. With a reduction in the brain 5-HT content, either by way of suppressing its synthesis with parachlorophenylalanine (PCPA) or by destruction of the midbrain raphe nuclei, the consolidation of temporary connexion is likewise disrupted, but under these conditions the disturbances of the consolidation process are, on the whole, not so severe as with the excess 5-HT in the brain. Overall, the research results thus obtained make it reasonably obvious that there exists a range of 5-HT concentrations in the brain necessary to permit the full-scale process of consolidation. Going beyond that range, especially towards higher 5-HT concentrations in the brain, violates the consolidation process and triggers the development of amnesia.

A special series of experiments, among them some conducted by our associate, Getzova, together with Vetzal and York from the Magdeburg Medical Academy's Institute of Pharmacology and Toxicology, GDR, reported an essential role for 5-HT in the regulation of protein synthesis and content in cerebral structures. In vivo and in vitro studies established an inhibitory influence of an excess 5-HT on protein synthesis in the hippocampus. With the aid of the methodology of cytointerferometry, it has been possible to discover that given an excess 5-HT in the brain, the change of protein content in the motor-cortex and hippocampal neurons takes a course directly opposite to that associated with training. Analysis of the research findings has identified a pattern of selectivity in the 5-HT-caused disturbances of protein metabolism that bear more immediately on learning and memory processes (brain-specific proteins, proteins of synaptic structures, protein receptors, etc.).

Presumably, this is the way 5-HT actually participates in the consolidation process.

Changes of catecholamine content in the brain are also a reported cause of dramatic disturbances in learning and memory processes. A decrease in the content of noradrenaline (NA) in the brain following inhibition of its synthesis by means of the inhibitor of dopamine- $\beta$ -hydroxylase, disulphiram, or through electrolytic destruction of locus coeruleus (LC) is the primary source of interfer-



ence with the elaboration of conditioned reflexes. Giving this, the scope and extent of the disturbances in the conditioning of particular reflexes is a function of their complexity. Indeed, the elaboration of more elemental conditioned reflexes appears to be less damaged by it than of more complex ones. For example, it proves next to impossible to elicit chain motor-feeding conditioned reflexes, whereas simple motor-feeding reflexes in the form of pushing at the door of the apparatus are produced with relative ease. Disturbances in the retention of the conditioned reflexes elicited against the background of an NA deficit in the brain are, as a rule, of secondary character in the sense that these disturbances derive as a consequence of the defective conditioning. The following observation serves to illustrate the point. An electrical skin stimulus, if not applied at once but some five or ten minutes after the mouse passes from an illuminated to darkened compartment, worsens considerably the CRPA retention 24 hours after the event (Table 2.5).

**Table 2.5.** Influence of 300 mg/kg Disulphiram Injection upon Defensive Conditioned Reflexes Elaborated in One Pairing with Delayed Reinforcement

Groups of animals <sup>1</sup>	Time of stay in illuminated compartment in initial experiment, sec ( $M \pm m$ )	Time of stay in illuminated compartment in retention checkout 24 hrs later, sec (ME)
5-second delay		
Control, $n=10$	$33.71 \pm 2.79$	300
Experiment, $n=10$	$40.80 \pm 2.17$	221
10-second delay		
Control, $n=25$	$31.10 \pm 1.79$	287
Experiment, $n=21$	$47.70 \pm 3.01$	157 <sup>2</sup>

<sup>1</sup>  $n$  — number of animals.  
<sup>2</sup>  $P < 0.05$  compared with control.

This observation, in conjunction with other known facts about the impairment of developed conditioned reflexes owing to an NA deficit in the brain, provides solid evidence, in support of Kety's hypothesis regarding the mechanisms of NA participation in learning and memory processes. According to the hypothesis, the NA evolved during the realization of reinforcement, prolongs the activity of those neurons which have responded to the presentation of a preceding indifferent stimulus.

One consequence of this is greater ease in starting connexions between the neuronal populations to which the signal (conditioned) and reinforcing (unconditioned) stimuli are addressed, that is,

greater ease in the initiation of temporary connexion (trace of memory).

Two essential indices with respect to the functional state of the noradrenergic system are NA secretion and reuptake (the key mechanism of inactivation) by nerve endings. They were just the indices employed by the author for his joint researches with Bazyan and Glebov, attempting to estimate the NA secretion and reuptake by the nerve endings obtained from the brain of rats in whom defensive reflexes have been conditioned. The use of  $H^3$ -NA in the research has allowed the revelation of a reduced capacity of the nerve endings (NA-synaptosomes) obtained from the rat brain upon conditioning of a two-way avoidance reflex, for high-affine (specific) NA reuptake.

Unlike them, the NA-reuptake capacity of the synaptosomes obtained from the brain of rats to whom the same stimuli (light and current) had been presented without pairing did not change at all. 30 minutes after the reflex conditioning was completed the capacity of the synaptosomes to reuptake NA returned to the initial level.

As to the NA secretion by synaptosomes, there were no changes at this point in time in the spontaneous secretion triggered by the reflex conditioning or presentation of unpaired stimuli. In contrast, with potassium depolarization of the synaptosome membranes, i.e. with the addition of KCl into the incubation medium, NA secretion from 'trained' synaptosomes grew faster and its extent was larger than for untrained synaptosomes. It is hence inferred that conditioning produces changes in the properties of nerve endings similar to those that also persist after the latter's separation from the brain and reveal themselves *in vitro*. These changes arise exclusively during conditioning and may well be treated as more or less specific.

Results of the studies already carried out attest that the functional state of the noradrenergic system is still rather high after another 30 minutes following conditioning. This finding suggests the double role of the noradrenergic cerebral mechanisms in the initiation of temporary connexions and in setting the stage for their full-scale consolidation.

A third line of research into the ways the noradrenergic cerebral mechanisms become involved in and contribute to learning and memory processes attempts to clarify the role of these mechanisms in the regulation of chemoreactive properties of the membranes of cerebral neurons.

Lately, there has been growing justification and acceptance for the concept that the initiation and long-term retention of temporary connexions is basically due to the stable changes in the chemoreactive properties of the neurons, brought about by a restructuring of their receptor machinery. This concept, initially highlighted

in a number of hypotheses, was then given the direct support of experimental data as the factors of changes in altering the chemoreactive properties of the membranes of cerebral neurons in the production of conditioned reflexes came to be known.

There is no way one can ignore, in the assessment of this idea and its underlying factual evidence, that the noradrenergic system of the brain is intimately related with the 'reward' and 'reinforcement' apparatuses. The study of the system's mechanisms of participation in learning and memory processes, and particularly investigation of its role as a regulator of the chemoreactive properties of

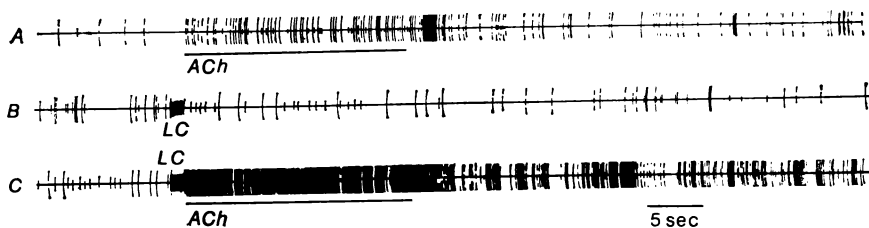


Fig. 2.5. Enhancement of response by hippocampal neuron to microionophoretic application of acetylcholine (ACh) following electrical stimulation (LC).

A—neuron's response to ACh application before LC stimulation; B—influence of LC stimulation upon the neuron's activity; C—response of the same neuron to ACh application following LC stimulation.

the neuronal membranes, is essentially identical with study into the mechanisms of reinforcement, the determinant factor in the rise and progress of temporary connexion.

These ideas were used as guides in a series of studies by this author in collaboration with Koshtoyantz, Eikel, Schmidt, Markarova and Kulikov. Their aim was to explore the impact of changes in levels of functional activity of the cerebral noradrenergic system upon the chemoreactive properties of neurons in the neocortex and hippocampus of alert rats immobilized by myorelaxants. To activate the noradrenergic system, two techniques were used: electrical stimulation of locus coeruleus (LC) and, in a special series of experiments, microionophoretic NA application to the neurons being studied.

Abatement of the functional state of the noradrenergic system was achieved through the suppression of NA synthesis by disulphiram or by electrolytic LC destruction 20 days before the experiment, this being the date when the NA content in the brain had sunk to its lowest. The studies found that changes in the functional state of the noradrenergic cerebral mechanisms entailed well-defined

modifications of the response by cerebral neurons to the micro-ionophoretic application of acetylcholine (ACh), dopamine (DA), and glutamate (Gl); e.g. following the LC stimulation, there came an observable, sharp increase in the response by hippocampal neurons to the ACh application (Fig. 2.5). In other instances the same LC stimulation weakened the AC responses (Fig. 2.6) instead of enhancing them. The summary data with respect to the influence of the LC stimulation upon the chemoreactive properties of neuronal membranes in the neocortex and hippocampus are cited in Table 2.6. They suggest changes of neuronal responses to ACh, DA

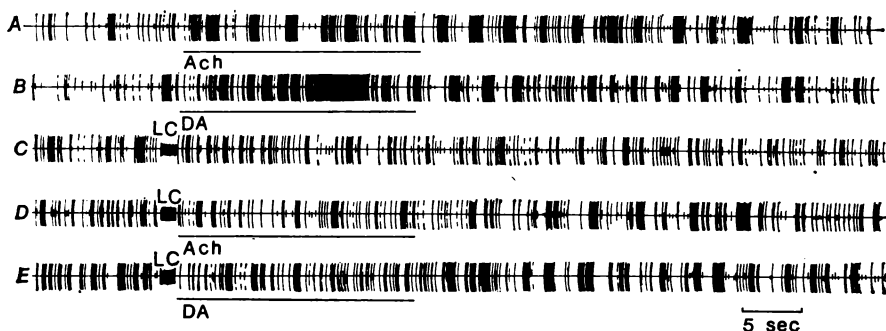


Fig. 2.6. Changes in responses by hippocampal neuron to micro-ionophoretic application of acetylcholine (ACh) and dopamine (DA), due to LC stimulation.

A, B, D, E—responses of the hippocampal neuron to ACh and DA application before (A, B) and after (D, E) LC stimulation; C—LC stimulation and its after-effect.

and Gl because of the LC stimulation in the great majority of the cases outlined. Significantly, the direction of the changes was in no way dependent upon the reaction of the investigated neuron to the LC stimulation. As may also be deduced from Table 2.6, modified responses to the application of the neurotransmitters came also from those neurons which have failed to respond to the LC stimulation. Essentially similar data were gained in experiments correlating the ACh, DA and Gl responses of cortical neurons before and after the NA application to them. The research findings substantiate two important conclusions.

1. The effect of NA, whether by excretion due to the LC stimulation or by microionophoretic application to central neurons, alters the chemoreactive properties of these neurons.

2. Readjustment of the neurons' chemoreactive properties is performed by the mechanisms whose activity fails to appear outwardly as changes in the impulse activity of the appropriate neurons. Prob-

**Table 2.6.** Influence of LC (locus coeruleus) Stimulation on the Response of Neocortical and Hippocampal Neurons to Microionophoretic Application of Neurotransmitters (Koshtoyantz et al., 1980)

Reactions to application of neurotransmitters and their changes after LC stimulation							
Type of reaction	Stimulation	ACh	Number of neurons with modified ACh responses post-stimulation	DA	Number of neurons with modified DA responses post-stimulation	GL	Number of neurons with modified GL responses post-stimulation
Neocortex							
Activation	7 (27)*	16 (69.5)	11 (69)	5 (49)	4 (80)	15 (60)	11 (73)
No changes	9 (34.5)	3 (13.5)	2 (67)	3 (41.5)	1 (33)	1 (4)	0 (0)
Inhibition	10 (38.5)	4 (18)	4 (100)	18 (69.5)	15 (83.3)	9 (36)	8 (89)
Hippocampus							
Activation	12 (26.5)	32 (71)	29 (90.5)	12 (31)	11 (92)	29 (80.5)	• 27 (93)
No changes	4 (9)	2 (4.5)	2 (100)	2 (5)	2 (100)	1 (28)	1 (100)
Inhibition	29 (64.5)	11 (24.5)	11 (100)	25 (64)	22 (88)	6 (6.5)	6 (100)

\* in parentheses — share of neurons in %.

ably, the readjustments just mentioned proceed on the basis of non-impulse forms of neural signalization. There are certain reasons to attribute the NA-caused readjustments of the chemoreactive properties of the neuronal membranes to the chemical form of the signalization which current conceptions depict as having an appreciably large role in the integrative activity of the brain.

The abatement of the functional state of the cerebral noradrenergic mechanisms by LC destruction or the suppression of NA synthesis was also accompanied by changes in the chemoreactive properties of the cerebral neurons.

This expressed itself in a relative rise (from 40 to 65 per cent) in the number of activated neurons and a relative drop (from 37 to 26 per cent) in the number of inhibited neurons in response to the microionophoretic ACh application. At the same time the number of non-reactive neurons also decreased (from 23 to 9 per cent).

Changes of chemoreactive properties under the influence of microionophoretic NA application were registered also in the neurons functioning in the situation of endogenous NA deficit, but in that case they had a different character to what they would normally have. Aided by factor analysis, it has been established that, while there are normally several factors of the readjustment of ACh responses after the NA application, there is only one factor of the after-effect of such readjustments. This was contrasted with animals with destroyed LC or those which received disulphiram, in both of whom the readjustment of the ACh responses and their after-effect is controlled by one and the same factor. Thus it may be suggested that the mechanisms driving the readjustment of the ACh reactions caused by NA application are different in the neurons, having to function for some time in a situation of deficient endogenous NA, from those in normal animals. Further evidence to substantiate this, at least in part, derives from the fact that the after-effect of the ACh application in the control animals hinges upon a factor that does not show through in the indices of the ACh responses. In the test animals, conversely, the factor responsible for their specific patterns of ACh responses appears in some ways to be related also to the after-effect of ACh application. For the reasons suggested, one may tentatively assume that the normal reaction to the application of neurotransmitters relies for its execution on one mechanism and the after-effect of these reactions, indicative to some extent of their retention, on another.

The participation of the neuromediatory systems in learning and memory processes involves both: the separate effects of the systems and their interaction. For an illustration of the previous statement it is useful to examine modifications of the effects of intervention on the activity of the cholinergic system against the background of a modified functional state of monoaminergic systems.

Relevant studies made use of conditioned reflexes of two-way avoidance. The first experimental session and the second one, seven days later, involved each presentation to test animals of 50 light-current combinations, recording the number of conditioned responses of avoidance and escape. This method revealed that administration of scopolamine to intact animals at 0.5 mg/kg did not

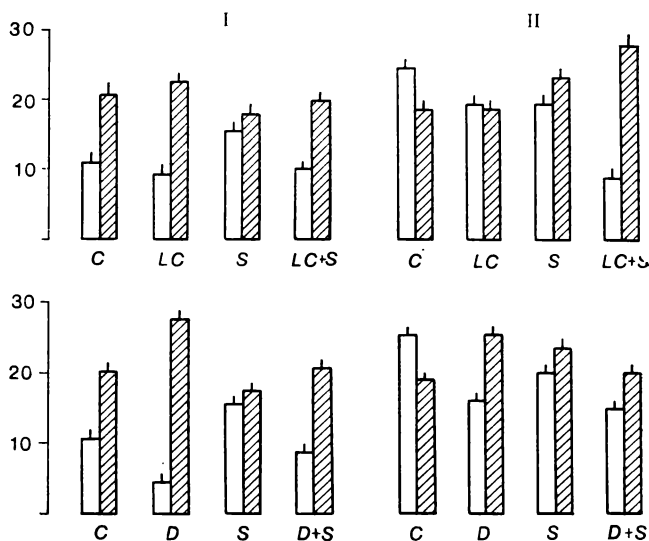


Fig. 2.7. Influence of reduced noradrenaline (NA) content in the brain upon the effects of scopolamine. Unhatched columns denote conditioned reactions of avoidance and hatched ones denote conditioned reactions of escape.

The ordinate is the number of conditioned reactions per experimental seance (I is the first and II the second experimental seance).

C—control; LC—destruction of locus coeruleus; S—scopolamine injection at 0.5 mg/kg; D—disulphiram injection at 100 mg/kg.

disturb the elaboration and consolidation of the conditioned reflexes. Nor did LC destruction, attended by the reduction of NA content in the brain, affect the elaboration and maintenance of the reflexes. However, when the same scopolamine dose was given to the animals with destroyed LC deep amnesia ensued. Interestingly, no such effects resulted from the reduction of the brain NA content by the suppression of its synthesis by disulphiram (Fig. 2.7). The modified scopolamine effects stemmed also from interventions into the activity of serotonergic cerebral mechanisms: in the animals having their cerebral serotonin content decreased through the suppression of its synthesis by parachlorophenylalanine, the 0.5 mg/kg sco-

polamine exposure induced complete amnesia. Another way of lowering the serotonin content in the brain—by destruction of the midbrain raphe nuclei—made no difference to the effects of scopolamine (Fig. 2.8).

These research findings indicate the unimpaired integrity and efficient functioning of the monoaminergic systems as a key condition for adequate performance of the cholinergic brain mechanisms and their resistance to adverse impacts, e.g. in the blockade of the ACh receptors. The differences that these studies made apparent

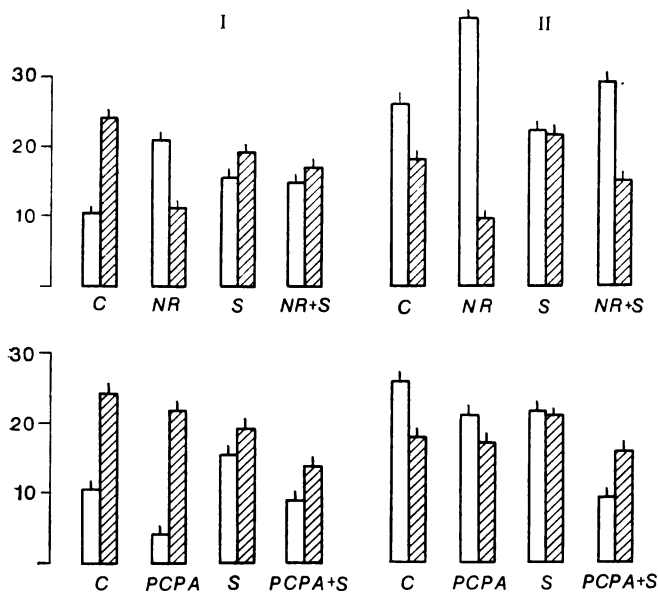


Fig. 2.8. Influence of reduced serotonin content in the brain upon the effects of scopolamine.

NR—destruction of midbrain raphe nuclei; PCPA—injection of parachlorophenylalanine. All other symbols are those of Fig. 2.7.

between the effects of pharmacological and surgical interventions indicate that changes in the functional state of the monoaminergic systems are brought about not only by a particular level of monoamines in the brain, but also by how that level has been altered.

To explore the interaction of monoaminergic systems in the course of learning and memory processes the activity of one of the monoaminergic systems was interfered with and the latter's effects investigated against the background of a modified functional state of another system. Suitable pharmacological and surgical treatments were used such as destruction of the midbrain raphe nuclei, LC destruction, and the application of drugs modifying the mono-



amine content of the brain. Their use has led to the identification of some sort of an asymmetric pattern of interaction between monoaminergic systems in the learning and memory processes. Intervention in the activity of the catecholaminergic system has a greater effect on the functioning of the serotonergic system than has intervention in the activity of the serotonergic system on the functioning of the catecholaminergic system. In other words, the catecholaminergic system is the one with a dominant role in the functional balance of the monoaminergic systems that exists in the formation and maintenance of conditioned connexions. This conclusion, prompted by factual data, gives further support to the key role of noradrenergic mechanisms in the integrative activity of the brain.

An investigation into the involvement of neuropeptides such as leu- and met-enkephaline,  $\beta$ -endorphine, lysine-vasopressin and its analogues, P-substance, ACTH<sub>4-7</sub> and ACTH<sub>4-10</sub> in learning and memory processes showed the effects of the injection of some peptides to depend upon the features of learning specific to the test animals. Of the peptides listed above, met-enkephaline was found to improve fixation of temporary connexions in the animals that are poor learners, but keep it unaltered if not downgraded in the animals that learn well.

Certain correlations have been found to exist between the influence of peptides on the processes of learning and memory and changes in protein synthesis in the brain structures. A clear example is improved retention of temporary connexions due to an analogue of lysine-vasopressin with concomitant enhancement in the incorporation of H<sup>3</sup>-tyrosine and C<sup>14</sup>-leucine into proteins of the hippocampus and several other cerebral formations. A parallel if somewhat opposite finding concerned potentiation of the effects of met-enkephaline following the activation of the catecholaminergic cerebral mechanisms by L-DOPA injection to the test animals. Unlike it, the activation of the serotonergic brain mechanisms by 5-HTP injection had no influence upon the effects of met-enkephaline. This evidence points unequivocally to the participation of the catecholaminergic mechanisms of the brain and the processes of protein metabolism in the mechanisms by which neuropeptides influence learning and memory processes.

Much attention has been paid recently to the benzodiazepine system of the brain and related quests of endogenous ligands for the benzodiazepine receptors. This takes place on the supposition that endogenous and exogenous benzodiazepines compete for a receptor so that the binding of the exogenous benzodiazepines to receptors can give at least some idea about the synthesis and release of the endogenous benzodiazepines.

Studies by our colleague, Korotkov, showed that the capacity of the synaptic membranes of the brain cortex neurons to bind H<sup>3</sup>-diazepam is modified by the elaboration of the defensive reflex or unpaired presentation of stimuli. His data reveal a maximum capacity for H<sup>3</sup>-diazepam binding in the synaptic membranes obtained from the brain of the rats exposed to unpaired stimuli. The reflex conditioning involves a less pronounced increase of the ability to bind H<sup>3</sup>-diazepam. The regularity shows itself over a wide range of H<sup>3</sup>-diazepam concentrations in the incubation medium. Apparently the H<sup>3</sup>-diazepam combination by the synaptic membranes varies proportionally to the degree of emotional arousal, which is stated in the Simonov information theory of emotions to be higher in the animals exposed to unpaired stimuli than in those which have developed a defensive conditioned reflex. It is not unlikely that the extent of synthesis suppression and the release of endogenous benzodiazepines and thus, consequently, the capacity of the synaptic membranes to bind H<sup>3</sup>-diazepam are all proportional to the intensity of the emotion of fear.

When combined, the data presented in this contribution corroborate its initial assumption of a great role for the neurotransmitter systems in learning and memory processes. It may be further suggested that the cholinergic and cholinoreactive systems of the brain have an equal measure of involvement both in the formation of the engram as well as its fixation. The catecholaminergic cerebral mechanisms appear to be more immediately related to the engram formation proper and the serotonergic ones, to the latter's fixation. But of course the neurotransmitters' 'non-transmitting' function of modifying the metabolism of macromolecules has a major part in their participation mechanisms of learning and memory processes. Finally, neuropeptides might also run the 'non-transmitter' function of the neurotransmitters to carry through their effects.

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# 3

## Multineuronal Analysis of the Systemic Function of Cortical Cells

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There is a wide-ranging debate in present-day physiology about how neuronal elements responsible for the organization of animal behaviour work. Livanov (1975), Asratyan (1965, 1970) and Kostyuk (1973, 1977) support the conclusion that, even though nerve elements may have been proved to be part of a particular reaction, this is still not enough to develop convincing ideas about the formation mechanisms of the integrative activity of the nervous system. Theoretical neurophysiology has effectively supplied the missing link by description of specific forms of nervous activity. For this the concept of system as a form of interaction of nerve elements was integrated into physiological definitions. The term 'system' gained broad acceptance and is currently utilized to mean very diverse things. Such a different interpretation of system, an extremely important concept for the understanding of neural mechanisms, makes it difficult to analyse specific experimental data, not to mention that on occasions it is thus stripped of its definitive role in the statement and resolution of neurophysiological issues. The necessity to specify the term 'system' is particularly imperative in the research into the mechanisms of behaviour, the most complex of the organisms's integrative activities.

In physiological science, the 'system' definitions—those actually including the word 'system'—have long since served as key concepts. Terms like 'nervous system', 'vascular system', 'muscular system' and most other terms provide traditional and fundamental ways of emphasizing specialized functions in general physiology. The differentiation of neural formations into systems is usually based upon the specificity of their tissue structural elements and the union of their function. In recent years the systemic understanding of physiological functions has become a scientific problem in its own right with its own hypotheses and tasks. The origination of the problem of systems analysis in physiology, and especially in the physiology of behaviour, was dictated by many factors. Two of them are worth special mention in view of their over-riding importance. The first refers to the rapid development of the so-called 'systems' approach in various scientific disciplines, giving rise to the scientific philosophical concept of a 'general theory of systems'.

The second factor is associated with the efforts of researchers to generalize the findings of the analytical investigation of functions based on possible forms of dynamical interaction between basic constituents of the process under investigation. In Soviet physiology there is a thoroughly elaborated theory of functional systems devoted to the interconnected activity of nerve structures for the organization of a certain goal-directed reaction (Anokhin, 1973).

Some authors identify a neuron-glial functional system in the cerebral cortex (Roitbak and Fanardzhyan, 1979).

In broad terms, the concept 'systems activity' applies to any nervous activity of whatever complexity. The activity may be afferent or it may be goal-directed. Two principles define nervous activity as systemic: (1) functional organization of the constituent structural units, and (2) definite ultimate effect. Any response to a signal is known to be composed of a series of successive forms of responsiveness. The first to be excited are receptors, in which the physical parameters of a signal are transformed into bioelectric parameters. The latter excite thalamic and subcortical centres triggering, on each analyser level, ever more complex processes of perception, processing and transmission of information. Ultimately, on the cortical level, the signal is 'recognized' in the specific projection zone. Depending on whether the signal is accidental or associated with a specific form of behaviour, new structural formations are recruited for the process. All of the just described cycles of perception and reaction to a signal can be thought of as a systemic activity involving the mutually coherent operations of various nervous structures. At the same time other processes occur on the level of individual structures which require the elements of a given structure to act in a mutually coherent manner and thereby ensure that the signal is subjected to a certain form of analysis. A system can thus be composed of several subsystems and the subsystems broken down into microsystems, depending on the complexity of the function discharged. Hierarchical gradation is essential for any systemic activity that reveals itself as a response of the organism to the environment.

The foregoing suggests a third principle in the physiological definition of systems: the level of systemic activity. Whether we speak about integrative behaviour or the activity of the afferent apparatus, or detail the operating mechanisms of an individual cerebral structure, it is still necessary to modify the content and research methods of systemic activity.

All these three principles of systemic activity, namely interaction of elements, ultimate effect, and hierarchical levels, are essential not only in the conceptual sense, but also to make the analysis of neurophysiological studies produce results. Interaction of components as a fundamental principle in the organization of a system

constitutes the key factor for experimental investigation of systemic activity. Any neural element, brain nucleus and so on can be integrated into a system's analysis if its activity is studied as a function of other components taking part in the system in question. This cardinal condition for the study of systemic activity excludes any other method employed in analytical neurophysiology (Kostyuk, 1973). Not infrequently, the axiomatic idea that the activity of any nervous substrate proceeds under the influence of an ongoing integrative reaction makes it possible to consider the substrate's functional readjustments as a result and an indicator of the organism's systemic activity. Essentially, this kind of comparison of a system's component with integrative systemic activity does not advance the understanding of the system's organization mechanisms because the interaction of a system's components, the major principle in the organization of the system, is thereby left out. The system does not interact with individual components, it rather consists of interactive components.

The ultimate effect is defined in large measure by the level of systemic activity. On the level of integrative behaviour, with numerous central and peripheral neural elements involved in the process, the effect may be a specialized goal-directed response. On the analyser level, this may be an evaluation of the physical and biological properties of a signal. Finally, on the level of nerve elements, columns of cortical neurons are said to exist responsive to modality-specific signals (Mountcastle, 1957; Hubel and Wiesel, 1965). Also by the criterion of ultimate effect some workers identify a group of neurons, the so-called barrels, which when excited cause, for example, the movement of vibrissae in rats (Loos, 1976).

It is therefore generally acknowledged that there exist macro- and microsystems whose workings seek to execute a definite function.

Thus, the system is a specific set of nerve elements which bring about a certain physiological effect if and when they act together; similarly, systemic activity is a form of interaction between nerve elements. When we examine a functional state of various structures in the accomplishment of an integrative reaction, the information we obtain first tells us about the participation of the structures in that reaction. With respect to a system, it may be said that by testing various elements separately we discover the structural make-up of the system. Yet the idea about the system's make-up has as yet virtually nothing in it to provide us with a clue to its functional organization or, in other words, systemic activity. If elements A and B enter into the system of K-reaction this still does not mean that the elements A and B exhibit systemic activity in the K-reaction, because participation may or may not be synonymous with interaction. The elements A and B may not interact or

may refer to different subsystems. Further, their interaction may be subordinate, and then the question arises about the type of interaction between them. One- or two-way, excitatory or inhibitory, interactions are all types of relations which offer a specific idea about the functional organization of a given system or the specificity of systemic activity. Indeed one may assume in theory what experiments confirm, that two elements may equally participate in different reactions in terms of ultimate result. While this is so, differentiated forms of an integrative reaction imply different specialized organization for the functioning of the nervous system, that is, specificity of the systemic activity of nerve elements.

Conceptions regarding the neuronal organization of the higher levels of the nervous system are based, first and foremost, on morphological description of the structure and synaptic contacts of central cells. Owing to the lack of dependable physiological techniques to investigate interneuronal connexions, current theoretical inferences about the organization of cortical neuronal circuits are in many ways hypothetical and do not lend themselves to objective estimation in experimental conditions. Laborious electrophysiological studies of connexions between neurons, aided by methods of microstimulation and intracellular recording, have failed to yield convincing results for two reasons. First, electrical stimulation may have stimulated synaptic inputs that are practically inactive, physiologically; second, the time course of the intracellular records is as yet insufficient to be able to follow changes in the synaptic connexions of the neuron examined in adaptive reactions. An essential shortcoming of the morphological conceptions has thus far been the failure to design measures of dynamic readjustment of interneuronal relationships or conversion of potential connexions into actual ones and vice versa.

When we say that a system begins with the study of the activity of the nerve element as a function of other elements, we actually touch upon the principles of organization of systemic activity and analysis of the basic factors contributing to its formation.

When, on the contrary, it comes to identifying a system as a set of interactive nerve elements which seek to get a certain function done when they act together, the point should properly address the composition and description of the system. It must be stressed that for a well-rounded characterization of a system, and especially a microsystem, one has to know not only the number of interacting nerve elements, but the ultimate effect of the elements' interaction.

Mountcastle (1957, 1978), Hubel and Wiesel (1965), Loos (1976), Batuev and Bambindra (1977), Batuev (1978) and Kogan (1979) describe in detail the structural and componential make-up of a neuronal system as it performs a certain analytical function. Nevertheless, none of the functional organizations of the systems they

emphasized, that is, systemic activity based on the interaction of the elements involved, has been confirmed to date with sufficient scope.

All of the assumptions discussed above require solid experimental proof. It can be stated, moreover, that the very problem of systemic activity still needs, on the whole, further elaboration as much as it needs the selection of suitable experimental techniques for its analysis and description.

Recognition of systemic activity as a form of interaction between the elements of a system necessitates the recording of the activity of several neurons simultaneously. Even though the activity of a multitude of neurons is not in itself an indicator of functional integration of the neurons, this type of recording is indispensable for the subsequent analysis of functional connexions between the neurons.

The literature contains detailed descriptions of methods for recording the activity of two, three and four cells of central structures in the nervous system (Verzeano, 1956; Amassian et al., 1961; Kogan, 1966; Efremova et al., 1967). The early period of multiple recording was marked by attempts to increase the number of microelectrodes inserted into the brain. Using specialized electrode holders, investigators attempted to insert into the brain (cortical and subcortical regions) simultaneously three or four microelectrodes. But the complexity of the search for and retention of a neuron by each electrode increased with the number of electrodes inserted. The electrode spacing, computed from the sinking angle and depth, proved also of concern. So finally one-electrode multineuronal recording has been generally recognized as the most promising procedure.

The methods, theory and ways of analysis of multineuronal activity are receiving much attention in the literature. It suffices to mention the multi-author works with entire chapters devoted to the recording and analysis of multineuronal impulsation (Bioelectric Recording Technique, 1973; Glaser and Ruchkin, 1976).

Multineuronal activity was first described by Strumwasser in 1958. He used a steel electrode with a tip diameter of 80  $\mu\text{m}$  to study neuronal activity in the mesencephalic reticular formation of the squirrel. Strumwasser greatly improved the technique of investigations into the multiple impulse activity of neurons; he abandoned the procedure of searching for neurons with a micromanipulator and brought into practice a chronically implanted electrode. The search was maintained exclusively within the operation time-frame. He reported the recording of multineuronal activity by a cement-fixed electrode for over a week. It thus became possible in experimental neurophysiology to monitor on a long-term basis, over several days, the activity of nerve cells in the brain of normal alert

animals. The method has great advantages for long-term research into the neuronal activity of the higher levels of the central nervous system, especially for the study of the neuronal mechanisms of learning. The chronic recording technique is currently used on laboratory animals such as rats (Olds, 1967; Olds, 1973), cats (O'Keefe and Bouma, 1969; Gassanov, 1971; Gassanov and Galashina, 1975), dogs (Cassady et al., 1973) and monkeys (Schmidt et al., 1976; Arezzo et al., 1977).

As the method gained ground, alternative methods for recording different-amplitude impulsation in chronic conditions were developed. John and Morgades (1969) developed a procedure for the recording of multineuronal activity via a 'moving microelectrode'. They tapped a microelectrode into a subcortical nucleus to the area with pronounced multineuronal activity and left it in that position for about a week until the impulsation disappeared. When the activity terminated, a miniature micromanipulator was used to move the electrode to a new active region.

At present, the method for recording multineuronal activity by means of rigidly fixed electrodes is widely used (Naka and Kido, 1967; Olds, 1973; Susuki, 1974; Gassanov, 1975). For this purpose metallic electrodes are usually employed with a diameter from 25  $\mu\text{m}$  to 100  $\mu\text{m}$ . Some investigators sharpen the tip down to several microns (Burns, 1974). As a rule, several electrodes (up to eight or nine) are implanted into the brain either in series (Olds, 1973; Burns, 1974) or as a bundle (O'Keefe, 1969; Gassanov and Galashina, 1975; Gassanov et al., 1979; Merzhanova, 1979). The electrodes are fixed on the skull with a cementing compound and their outer terminals are soldered to the connector. It appears as if the large number of electrodes compensates for the absence of their freedom of manoeuvre. With the electrodes rigidly fixed, the investigator is not free to move them about in search of the active point after the operation. Then the advantages of implanting numerous electrodes come to the fore.

Experience has shown that two or three out of seven to nine rigidly fixed electrodes find impulse activity. On rare occasions it is possible to record multineuronal activity with the majority of the electrodes. In some cases, however, no impulsation is found.

Burns et al. (1974) performed quantitative analysis on the 'working capacity' of chronically implanted electrodes and emerged with a conclusion essentially identical with our own. Of all implanted electrodes, about one third show the activity of the alert state, just as one third of the working points yield long-term activity.

Long-term recording of neuronal activity from rigidly fixed electrodes reveals a number of interesting and new experimental phenomena. The duration of the active state underlying one electrode is measured over a range from several days to several months. Cha-



rover and Deluca (1972) recorded multineuronal activity from the olfactory bulb in rats in the course of three months and hypothesized, from the shape of the spikes they obtained, that the neurons remained the same throughout. Schmidt\* et al. (1976) recorded multineuronal activity from the motor cortex at eleven points for 233 days in one monkey and in another monkey twelve points were working for 141 days.

Guided by the spike shape, type of receptive fields and the pattern of discharges, these authors suggested that one neuron could work for as long as 29 days. Within that period, stable registration was observed for eight days, indicating the periodical pattern of neuronal activity. Somewhat earlier, Gassanov and Galashina (1975) published data on periodicity in the activity of auditory cortex cells in cats with chronically implanted electrodes. These researchers identified the neuron by the pattern of the post-stimulus histograms on exposure to sound stimuli.

Another fact obtained from experiments with multineuronal recording concerns the shape of spikes. Usually, all impulses, whatever their amplitude, have two, less often three, phases, and only on rare occasions are they monophasic.

As noted above since the 1950's multineuronal activity has attracted the attention of researchers. And, despite the intervening thirty-years period since the pioneering investigations in that direction and the method's increasing scope over the past few years, multineuronal activity recording meets with reserved, indeed sometimes critical, attitudes. Verzeano (1973) quotes some of the more frequent criticisms levelled against multineuronal research procedures, which the author rejects absolutely. The criticisms decry the unclear nature of multispike impulsation, difficulties of identifying an individual neuron in such a record, and other disadvantages.

Evidence from literature, along with our data, make us reasonably sure that the major difficulty in the analysis of multineuronal activity arises whenever an attempt is made to separate the impulsation of the individual neurons comprising this neurogram. The complex form of the impulses and the broad spectrum of their amplitudes are coupled with high-level neuronal noise to yield a picture commonly considered as an unclear recording.

There exist several ways of differentiating impulse series from a multiunit record. The simplest of these is by division of impulse trains according to horizontal level. This is done with discriminators that separate out the impulses above a given level. The method can help obtain a series of transformed impulses corresponding to the spikes with the largest amplitude, if the level is set up high above the noise level, or a series of different-amplitude spikes, if the level of discrimination

runs somewhat lower. For the low-level discrimination, it is possible to integrate into one train of transformed impulses the discharges of all recorded neurons (Berry et al., 1978). Applications for this method in the analysis of multineuronal activity are relatively few because such discrimination fails to provide for the separation of individual discharges on the basis of their amplitude with the exception of the largest spikes.

The method's inherent disadvantage is eliminated if the spikes are discriminated by their amplitude, using band discriminators that impose constraints on both the lower and the upper levels. This discrimination of separated impulse series by the 'window' is at present widely applied in electrophysiology. Introduction of the amplitude discrimination method as a routine tool of multineuronal research encouraged the development of work on statistical approaches to the analysis of the impulse activity of neurons. On the other hand, the new scope for the amplitude discrimination techniques raised several issues of principle.

The first to arise was the question about the boundaries of amplitude oscillations of the spikes generated by one neuron. On some estimates, the oscillations account for 25 per cent of the total (Burns et al., 1974). Some critics of the multineuronal method of recording question the validity of the judgement about the activity of an individual neuron based on the amplitude parameter alone, with no regard to the spike shape. For that very reason most of the studies now underway in that area include amplitude discrimination with close attention to the shape of the discriminated spike series. This is achieved by periodic recording of individual spikes on a high-speed CR sweep throughout the experiment (Fetz and Baker, 1973). As an additional criterion for sampling the impulses of one neuron, it is useful to employ the histogram of expectation density (autocorrelogram) or interval histograms that can give an idea about neuronal refractoriness.

Sampling of an impulse train of an individual neuron by the spike shape is held to be a more advanced method. For this a spike of standard shape is fed into a computer with sufficient storage capacity and similarly shaped spikes are separated from multineuronal activity on that basis. Swartz et al. (1976) discuss in great detail the reliability of spike discrimination in a multineuronal record. They seem to have agreed that errors in spike sampling by shape are likely to include undersampling the impulses of one series or oversampling—when spikes of two neurons are mistaken for one series. They propose their own method of sampling the activity of separate neurons based on a histogram of the amplitude spectrum of a multineuronal record. From the histogram, mean and sample standard amplitude deviations are computed and the width of the discriminator window estimated in order to identify the neurons

by the peaks of the amplitude spectra. Poststimulus histograms of the series that selected provide an additional means of control over sampling accuracy. With the proper sampling the histograms of response reactions have shown differences in their patterns.

Vibert and Costaj (1979) came to develop a preference for three parameters of the action potential as being the most meaningful ones in computer sampling: amplitude of the first phase of the action potential, amplitude of the second phase and width between their respective peaks. The results of processing multineuronal activity strongly suggest that strict theoretical requirements might not always be necessary with that kind of analysis. We shall provide an example from Verzeano et al. (1970) who recorded multineuronal activity in the lateral geniculate body and dorsal hippocampus of immobilized cats for studying the influence of metrazol on neuronal activity. By means of a system of discriminators, the whole mass of multineuronal impulsation was divided into six sequential levels. Significantly, such criteria as spike amplitude and shape were not among the authors' guides in that exercise. The analysis of the multineuronal activity demonstrated that low-level spikes disappeared after metrazol injection, medium-level spikes changed their frequency, and large spikes did not alter. Particularly intriguing, however, was the appearance of new spikes far exceeding in amplitude all of the other spikes.

In that experiment the findings go far beyond our current capabilities in microelectrode research. First, the small spikes that are always dismissed from microelectrode investigations on account of being a poor indicator have been actually the ones with maximum reactivity in relation to the pharmacological agent. Second, keeping the microelectrode constantly targeted on the active cell usually excludes the possibility of watching new neurons become active during the period of recording. Third, even the conventional subdivision of spikes by the amplitude criterion permits identifying selective influence on behaviour of the neurons. One can cite studies in which spike changes in the course of multineuronal activity were watched and estimated visually, without so much as sampling the spikes.

Naka and Kido (1967) offer records showing clearly, in the cat hypothalamus, the suppression of medium spikes and retention of smaller ones as the cats were shown a mouse. But once the mouse was taken away, large spikes appeared. Kasimov and Gassanov (1977) watched large spikes emerge in the rabbit amygdala under induced (by sodium chloride injection) and natural water deprivation. These experimental data illustrate the relative nature of the neat sampling of impulse series. One is therefore justified in assuming, as the criterion for neuron sampling, not only certain parameters of their action potentials, but also the effect of function-

al influence upon the separated impulse series, i.e. the result of an experiment.

Multineuronal recording of impulse activity has become widely used in recent years. The mounting research interest in that particular method of neuronal recording is to be credited to several interesting properties that are hard, if not impossible, to identify in the functions of single neurons activity. What are the properties?

*First property.* Any attempt at an objective assessment of functional interrelations between two neurons, and especially neurons of the neocortex, necessitates estimation of the distance between them. The chance finding of neurons in the absence of exact notions about their spatial disposition makes the comparison of temporal parameters in the activity of each neuron much less valuable. If an inhibition response of one cortical cell coincides in time with excitation of another cell, the interrelation of these two forms of impulse activity is the more problematic, the less we know about their relative position in space. To obviate these difficulties, it is usual to manipulate two electrodes so as to minimize the spacing between their tips once a definite depth has been reached.

However, even this approach has not been sufficiently adequate to answer the question about possible, much less real, interrelations of cortical neurons. For one thing, the accuracy of the resolution in determining the proximity of neurons by the method of converging electrodes is not always fine enough for reasonable certainty about the spatial interrelations between the neurons. For the distances between two neighbouring neurons may well measure in microns or tens of microns (Batuev and Bambindra, 1979; Burchevskaya, 1979). For another, the probability of two microelectrodes landing in the field of impulse activity is very low. Multineuronal recording, i.e. the recording of several neurons with one electrode, serves as a reliable tool for monitoring the activity of neighbouring neurons, the distance between them dictated by the density of their disposition in tissue volume. Using the method of chronically implanted electrodes one gains significant extra time to watch the combined operation of neighbouring neurons, lasting several days or weeks. In conclusion, the method offers a comparatively simple and nonetheless reliable and long-term way of recording simultaneously several neighbouring close-spaced neurons—an objective somewhat difficult to achieve with other recording techniques.

*Second property.* Multineuronal activity is often thought of as the activity of neighbouring but randomly scattered neurons relative to the electrode tip. This view received broad recognition and is perhaps the reason why multineuronal recording is often used as an economical means of recording a set of neurons.

Another, and also widespread view of multineuronal activity describes it as an indicator suggestive of the functioning of a neuro-

nal pool. In that event, the spatial analysis of the pooled neurons is thought to be of no special consequence.

Nevertheless, a more detailed perspective on the action potentials as they appear in multineuronal recording provides some rather significant insights into the structure of the neuronal pool being recorded. As a rule, in a multineuronal record all impulses are bi- or tri-phased. The initial phase, furthermore, is of high-speed and minimum in duration whereas the second phase is somewhat



Fig. 3.1. Form of action potentials in a multineuronal record. The motor cortex of a normal alert cat. Recording through chronically implanted electrode (nichrome) 50  $\mu$ m in diameter. Downward negativity.

extended over time. The third phase, if any, is usually of low amplitude but of maximum duration. The form of the action potentials such as this is well-known and in a multineuronal record the potentials appear with different amplitudes.

One cannot fail to see that, in a multineuronal record, the action potentials of different amplitudes have similar forms as concerns the direction of the phases (Fig. 3.1). Whatever the amplitude of the spikes in a multiunit record, all the initial phases (and, accordingly, the secondary phases also) possess the same polarity. Proceeding from the generally accepted idea of the action potential as being form-dependent upon the neuron's orientation relative to the electrode tip, one will have to assume the similar orientation towards the electrode for all neurons recorded in a cortical microlocus. This is an altogether legitimate assumption to make as long as the electrode keeps recording a group of closely adjacent neurons. There is ample morphological evidence suggesting the normal pattern of cell disposition in clusters for the neocortex, particularly its lower layers—the usual locus from which to record multineuronal activity. There are also indications that each cluster may hold from three to seven or nine cells (Batuev and Bambindra,

1977; Burchevskaya, 1979; Amassian et al., 1961). Hence it follows that multineuronal activity, under certain conditions, reveals the activity of spatially isolated microgroups of cortical neurons located in the immediate proximity of one another.

It is not unlikely, as experimental facts indicate, for a multineuronal record to pick up by chance also the action potentials of opposite polarity. The basis for such incidents is that the electrode

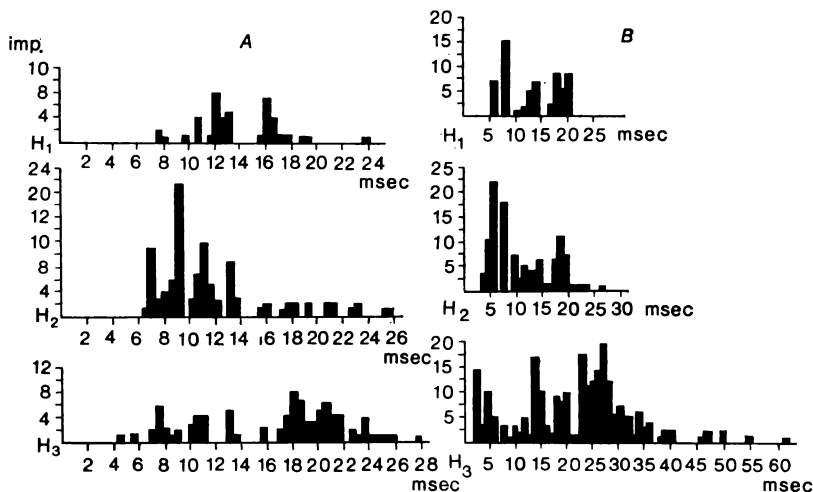


Fig. 3.2. Evoked impulse activity of neurons in the sensomotor cortex of immobilized cats produced by stimulation of the ventrolateral thalamic nucleus. The multineuronal activity was recorded via glass microelectrode. H1, H2 and H3 are poststimulus histograms, respectively, of large, medium, and small neurons according to spike amplitude.

comes into a position enabling it to record the activity of individual remote neurons. Normally, however, most of the spikes with different amplitudes in a multineuronal record will have a unipolar orientation, while the impulse series of the opposite orientation is comparatively rare. Consequently, the one-electrode recording of a neuronal set, particularly using a large tip diameter electrode (Manyanin et al., 1979) actually records the activity of local group of closely adjacent neurons.

*Third property.* Structurally, multineuronal activity consists of impulses having different amplitudes. In fact the number of recorded neurons can be estimated from the number of distinct amplitudes. On the basis of experiments with microelectrode investigations of a single neuron, in the literature the concept has been developed of the action potential as a function of the distance between neuron and electrode tip (Storozhuk, 1974). Subsequently,

the viewpoint of the different-amplitude recording of impulse activity which one electrode was adopted by many investigators, who came to see it as the activity of several neurons situated at different distances from the recording electrode. On the other hand, an analysis of the impulse responses to stimulations discloses a suggestive relationship between the character of evoked responses from the separated neurons and the amplitude of their generated charges. In our laboratory Weber, Stashkevich, Rapoport and Silkis have shown that the responses of neurons with low-amplitude impulses commonly have short latency but are, not infrequently, extended over time. The neurons with high-amplitude impulses yield responses having relatively longer latent periods and phasic in type (Fig. 3.2). If the amplitude of the impulses independent of the type of registration were strictly correlated with the electrode-neuron distance, the probability of the appearance of any form of evoked responses would be equal for the spikes recorded with large or small amplitudes. Obviously, the concept of amplitude as an index of the neuron's remoteness from the electrode does not hold for the incidents of multineuronal activity. It has to be acknowledged that in the multineuronal activity recording environment, specifically because of the capability of picking up impulses from a tightly organized group of neurons, it becomes possible not merely to watch the activity of several neurons simultaneously, but also to differentiate them according to the functional properties. In any case, the amplitude of spikes appears as a neuron property that is reversely related to their excitability. Low amplitude impulsionation is specific to the more reactive of the neurons and high-amplitude impulsionation to less reactive ones (Henneman et al., 1965). The intermediate amplitudes are common for the neurons in the midway position according to reactive properties.

As is known, the amplitude of impulses in multineuronal activity may vary in absolute measurement (Fig. 3.3). The signal-to-noise ratio should most probably be accounted for by the position of the recorded neuronal group relative to the electrode. In that respect, the principle of spatial relations acts in the same way as in microelectrode studies. The only difference is that, for a single cell, the distance is determined from one impulse parameter and in recording a neuronal set this determination involves the absolute amplitude parameters of all impulse series. With such an approach, the relative correlation of the amplitudes in a multineuronal record remains functionally important for the differentiation of neurons, irrespective of the absolute values of these amplitudes.

Publications of recent years supply plenty of data on the morphological identification of cells in the central nervous system based on the magnitude of impulse discharges. A variety of analytical techniques are marshalled to confirm the arguments for the

view that the spike amplitude can be indicative of the cell size. It is presumed that the higher the spike amplitude, the larger are the cell's dimensions (Henneman et al., 1965 [a, b]; Grover and Buchwald, 1970).

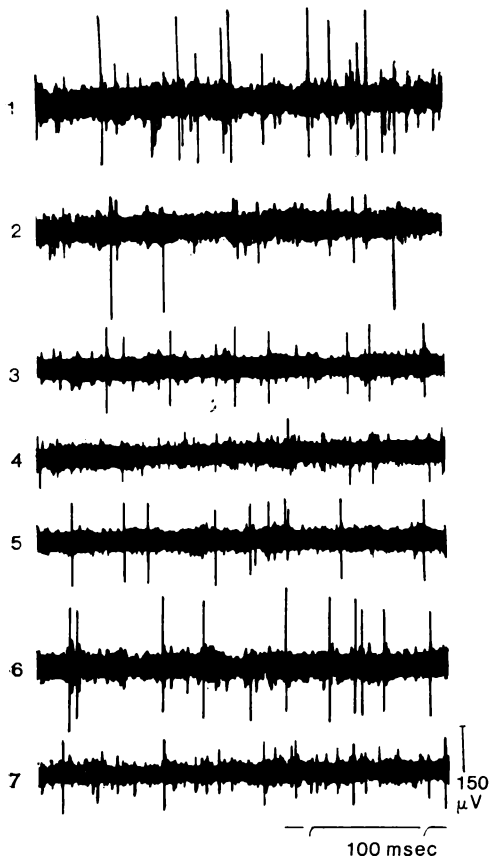


Fig. 3.3. Multineuronal records in the auditory cortex of an alert cat registered from several chronically implanted electrodes (nichrome) 50  $\mu\text{m}$  in diameter. Figures are numbers of glued-up electrodes.

two or three phases. As reported from acute experiments, monophasic activity occurs either with a large distance of the neuron from the electrode tip or when the electrode comes into contact with the neuron (Storozhuk, 1974). Bi- or tri-phased spikes occur when

The concept is justified for the functional description of multi-neuronal activity, from which large-, medium-, and small-size cells can be separated on the basis of some of their properties. A special analysis of the neuron size versus the spike amplitude goes a long way to substantiate the validity of this identification. As an example of the case in point the multi-neuronal activity of the auditory and motor cortex serves well. On morphological evidence, the auditory cortex contains cells of smaller size than does the motor cortex. The respective neurograms show a higher signal-to-noise ratio for the motor relative to the auditory cortex (Fig. 3.4).

Therefore, the differentiation of spike trains according to their amplitudes allows one to perform morpho-functional identification of cortical neurons, to yield the classes of large, medium and small neurons.

*Fourth property.* Ordinarily, the impulses in multineuronal activity have



the electrode is found at an optimal distance from the cells, that is, the distance permitting reliable and accurate recording of the neurons' discharging activity while, very importantly, leading to neither mechanical stimulation nor impairment of the target cell.

*Fifth property* concerns multineuronal activity being recorded from chronically implanted electrodes. The method of implanted electrodes provides an opportunity to monitor for days the impulse

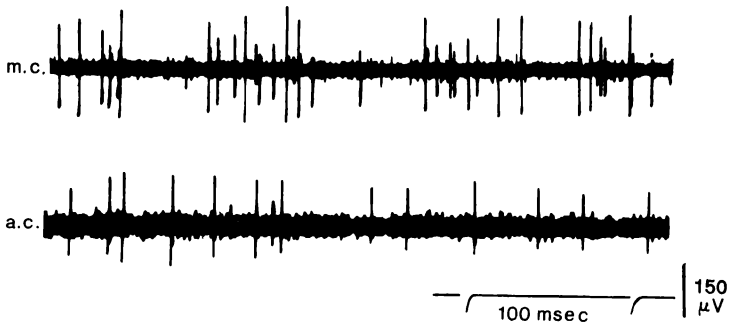


Fig. 3.4. Characteristic signal-to-noise ratio of a multineuronal activity recorded in the motor (m.c.) and auditory (a.c.) cortex of an alert cat. The chronically implanted nichrome electrodes have 50  $\mu\text{m}$  diameter.

activity of cortical neurons without time being wasted in search for the active points. A specialized analysis of impulse trains based on the form of the action potential or PSH has revealed the constancy of the investigated criteria, suggesting the ready availability of the same cortical neurons for observation over several successive days.

Contemporary neurophysiology is as yet short of data to hypothesize on the patterns and peculiarities of this several-day activity of cortical neurons. The method of chronically implanted electrodes opens up new opportunities in that area. In any case, experimental facts for the periodicity of cortical cells functioning have already been obtained and the presumability of active and inactive states found to be different for different cells (Gassanov and Galashina, 1974).

The capability for retention of the same neuronal group over a long time and with a high reliability enables the functional state of cells to be followed in a situation where the nervous system is influenced by pharmacological or prolonged afferent exposure. Of specific interest in that context is the change of neuronal noise with the use of chronically implanted electrodes a few microns in diameter. The effect of anaesthesia causes a sweeping reduction in

the magnitude of this neuronal noise, sometimes to several times less than the initial level (Bogdanov, 1979). These data offer a way to evaluate the functional state of small neurons whose recording is practically impossible though their activity generates the so-called neuronal noise in multineuronal recording.

The aforementioned properties of multineuronal recording all seem to lead to a conclusion that has a direct bearing on the morpho-functional characterization of elementary groups in the neocortex. The morphological data suggest the pattern of neuronal distribution in clusters in the various cortex layers. These neuronal groups are especially common in the lower layers of the cortex. Another circumstance is also noteworthy that some authors do not treat the neuronal microgroups as a component part of the vertical cortex columns (Peters and Walsh, 1972; Batuev and Bambindra, 1977).

In composition, the microgroup of cortical cells conjoins neurons of different types. The usual description of such a microgroup portrays it as consisting of one large pyramidal cell with medium- and small-size pyramids centred around it (Batuev and Bambindra, 1977; Burchevskaya, 1979). In terms of structural characteristics, the group unions of cortical neurons may well be seen as a microsystem, which, according to some investigators, should fulfil some elementary function.

Using the multineuronal method of recording, individual microsystems can be made the target of a physiological analysis. It should be noted specially that a detailed discussion of the properties of multineuronal impulsation shows the coincidence of findings between physiological and morphological investigations as to the pattern of cortical cell distribution in groups. On the parameter of spike amplitude, the identification of neurons is consistent with the morphological pattern of the microgroup. From the reactivity of the identified neuronal classes one can form an idea about functional differences among large, medium, and small neurons. And yet all the classificatory characteristics that describe the constituent elements of the microsystem of cortical neurons leave open the question about the interaction among these elements or, to put it another way, the systemic activity of neurons within the micropool of the neocortex.

The differential analysis of multineuronal activity provides the raw material for the subsequent statistical investigation of inter-neuronal relations. This and the more elaborate and improved special mathematical procedures now available have set the stage for a new and objective approach to the systemic activity of neurons.

Gerstein (1970), Dickson and Gerstein (1974) and Moore et al. (1970) offer thorough-going descriptions and discussions of the methods to deal with cross-interval interrelations of impulse trains from two neurons. Unlike the cross-correlation relations between two impulse trains, cross-interval relations are to be determined, not at macroplots of impulse series, but at micro-intervals of

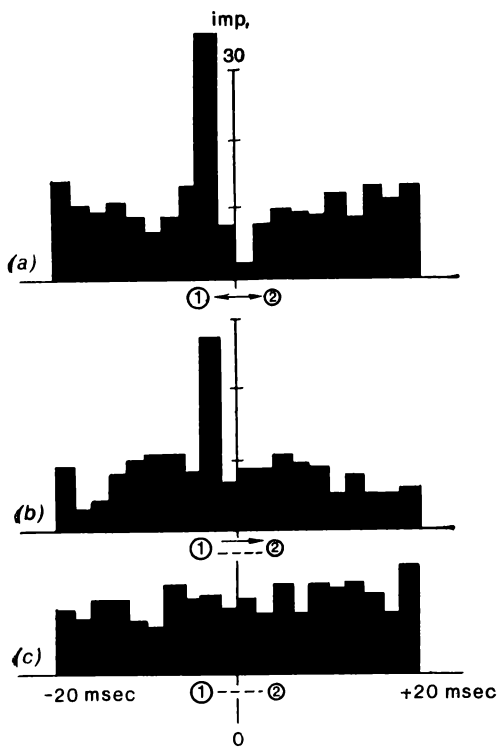


Fig. 3.5. Types of interrelations in neuron pairs. Each histogram consists of two cross-interval histograms, obtained on the analyser and made coincident relative to zero.

A—two-way asymmetric connexion, with the large neuron exerting excitatory influence on the small neuron and the latter inhibiting the large neuron; B—one-way asymmetric connexion, with the large neuron exerting excitatory influence on the small neuron and the small neuron operating independent of the large one; C—two-way independence in the activity of a neuron pair. Figures in the circles denote the large neuron (1) and small neuron (2). The set of impulses of the large neuron relative to the triggering impulses of the small neuron is presented on the right side of zero (+20 msec), and the set of impulses of the small neuron relative to the triggering impulses of the large neuron is cited on the left side of zero (—20 msec).

time relative to the spike of the selected series. For the postimpulse relations, temporal sequence in the analysis of neurons is material; in fact, it makes all the difference from cross-correlational parameter, which is independent of the sequential order of impulse series.

The method of building cross-interval histograms recalls in many ways that for the poststimulus histogram, but with the difference that the function of the stimulus in the cross-histograms is taken by each impulse in one of the series combined. A computer with a large storage capacity can produce a histogram with statistical feedforward and feedback. The relation that demonstrates dependence (or lack of it) of neuron B upon neuron A is labelled by the sign of plus and the inverse relation (A upon B) by the sign of minus. A histogram with

an identical type of statistical dependence on both sides of zero is considered symmetrical. The time of analysis is chosen arbitrarily and may reach several hundred msec. Bin width varies from tenths of msec to tens of msec.

The underlying principle of the cross-interval histogram is essentially one of bin filling probability by the impulses of the read-out series versus each (triggering) impulse of another series over a specified length of time (time of analysis) (Fig. 3.5).

The use of different time-of-analysis periods enables the identification of dependent relations both over short and long intervals. In the process, it must be possible therefore to monitor the frequency of cross-intervals of different orders. In cross-correlation histograms, however, the index of dependence appears usually near the zero time and reflects predominantly the intervals of the first order. This view is further supported by statistical data in which, given a long cumulation time relative to 0, the moment when the controlling spike is emergent, dependent relations occur, as a rule, in the initial part of the histogram. For an example, one can refer to Gerstein's article (1970) where a histogram with a 300 msec time of analysis is cited and a statistical relationship shown between two series of impulses in the initial bins.

A scrutiny of first-order cross-interval histograms can be carried out with comparatively simple electron summator built on the analyser model (Gassanov and Galashina, 1975; Krekule and Skvaril, 1976). This is achieved by setting the analyser regime to the mode of the postimpulse histogram and feeding first-series impulses, which initiate the analyser beam, into the nest of external synchronization and second-series (read-out) impulses into the cumulation nest. The analyser beam is triggered by each impulse of the first series and the cumulation is done over the time separating impulses of the first triggering series.

In view of the latter fact the recurrence rate of analysed impulse series becomes critical. Indeed, an impulse train with short inter-impulse intervals is very likely to trigger the analyser beam much too often, causing an accumulation of the read-out series impulses in the first bins and, consequently, an incorrect dependent relation. To avoid incorrect conclusions, the time of analysis for cross-relations should be determined from the least interval in the triggering series. This requires an interval histogram to be built or, alternatively, an electron gate to be used to block the input for the synchroimpulse.

Cross-analysis is now a widely used method of analysis because of the clear-cut description it provides of the quantity and quality of the histograms obtained. It is valued most, however, as a technical tool for an objective assessment and description of dynamics in the systemic action of neurons. On the other hand, the statistical approach raises a number of theoretical issues whose solution may add a significant new dimension to the physiological content of quantitative indices.

As is known, a statistical relationship between two events is as much controlled by the interaction of the events as by the influence upon them from an extraneous common source. The concept is a basic essential if an understanding of the joint activity of neu-

rons is to be developed. The statistical method of cross-analysis of impulse trains provides a convincing and demonstrative perspective on the major distinctive features of neuronal system function but, once again, it leaves open the question about a third source and therefore mechanisms driving the correlated activity of neurons.

There are studies in the literature devoted to a discussion of the possible neurophysiological processes underlying a temporal relationship between two impulse trains. Moore et al. (1970) analyse methods suitable for direct research into the synaptic interaction of neurons. They discriminate between two expressions of the cross-correlation function referred to respectively as primary and secondary effects. The primary effects represent the peak and trough close to the onset on the histogram (near the zero mark). Their amplitude, direction and shape, chiefly a reflection of the corresponding synaptic processes, are relatively independent of the ongoing impulsation of the analysed cells. They grow out of mono- or polysynaptic interneuronal connexions, excitatory or inhibitory, or else are due to the common inputs to these neurons from a third source. The authors maintain that the differentiation of the neuronal interaction and the common source can be made using the picture of secondary effects, which follow the primary and appear as periodic oscillations on the histogram. The post-synaptic periodicity finds expression only on the plus side of the histogram for the case of a monosynaptic connexion and on both sides of zero for the common input alternative.

Dickson and Gerstein (1974) treat the question in the following way. The common input option is relevant should similar dependent relations emerge on both sides of the histogram's zero point. If, however, their dependence is unilateral, this judgement is based on the temporal parameter of the dependent relation. Faced with a time-extended peak (or inhibition), one can speak of the common input. A narrow unilateral peak suggests an immediate interaction between neurons. Dickson and Gerstein (1974) are of the opinion that the common input exerts a synchronizing influence on two neurons, making them start discharging at about the same time.

The third source spans a wide range of influences. The likely candidates for such a source include blood constitution, temperature, blood pressure, ephaptic distribution, activating influences and a third regulating neuron or thalamic relay nucleus (Moore et al., 1970; Fetz and Baker, 1973).

All of the conceptions for the functional meaning of the neuronal interaction recognized from statistical indices rest essentially upon data obtained from model experiments based on the use of computers or very simple objects. The existing views and supposi-

tions with respect to the differentiated understanding of cross-interval histograms undoubtedly enrich the statistical description of system neuronal activity with concrete physiological mechanisms. But they also emphasize the need to continue the search along these lines for additional argumentation to support the common input concept or, alternatively, that of immediate neuron interaction. The authors themselves insist that their propositions have yet to be proved absolutely. Nevertheless the cognitive value of performing statistical analysis on interneuronal relations is unquestionable.

It is not merely that wide agreement on certain cross-histogram forms as relevant indices of interneuronal connexions opens up new horizons for the study of specific ways in which neurons are interrelated. In addition, it provides investigators with an easy-to-apply analytical technique in dealing with the synaptic mechanisms of that interaction. For confirmation, one may refer to studies containing discussion of the monosynaptic connexions between cortical neurons on the basis of cross-histogram data. One such, by Renaut and Kelly (1974), investigated pyramidal neurons in the precruciate cortex of a cat, only to find that some of them were inhibitory. On the theoretical assumption of correspondence of the asymmetric relations between two neurons to the immediate connexions and of the symmetric ones to the common input, they inferred that inhibition could be imposed both mono- and polysynaptically. Kimura et al. (1976) also considered the asymmetric cross-histograms as indices of neuronal interaction and symmetric histograms as the common input. They investigated neurons in the cat visual cortex with their preidentification from responses to a moving stimulus. In all pairs, the positivity (excitational dependence) was symmetric. The authors concluded that the neurons had been excited from the common input through the connexions from the lateral geniculate body. Only in four pairs out of the 48 in the sample frame did they detect an inhibitory monosynaptic connexion between neurons, as suggested by data of cross-analysis. In both studies the presumed monosynaptic connexion was recognized by a delay of the dependence index within the range of 0.6 to 2.0 msec.

To sum up, the concept of the asymmetric histograms as indices of neuronal interrelation seems to be the best-grounded at present and the most promising for the future. Statistical studies into the interrelations of two impulse trains have discovered one more fact of direct interest for the physiological perspective on the cross-histograms.

Many studies point out that dependent relations are often observed between neurons spaced 300 to 350  $\mu\text{m}$  from each other.

Dickson and Gerstein (1974) examined cross-relations in neuro-

nal pairs in the cat auditory cortex. A statistical relationship was traced for 95 per cent of the neuronal pairs covered by one-electrode recording and 35 per cent of the pairs recorded with two electrodes. In the latter instance the most important was the distance between the electrodes. The increasing distance caused the number of the correlating neurons to decrease; with the electrodes more than 1 mm apart, the relationship did not show up.

The effect of distance was discovered also in a study on medullary neurons in the cat (Vachon and Duffin, 1978). Of the 29 neuronal pairs recorded by two electrodes variously spaced from 1 to 4 mm from each other, only three exhibited the dependent relations. Analysis of the seven neuronal pairs recorded by means of one electrode revealed the dependent relations in five of them. The striking fact about these relations was that in distant neurons the relations, if any, were excitatory, whereas in the neighbouring neurons four of the relations were inhibitory and only one was excitatory.

The assumption that seems most probable from the above evidence is that the cross-correlations reflect the density of interneuronal connexions. If there exists a hypothetical third source, presumably as a regulating neuron or an extracortical source, the principle of reciprocity is ruled out as regards intercortical connexions (Szentagothai, 1970; Szentagothai and Arbib, 1974).

Asanuma and Rosen (1973) provided data that are as interesting as they are unique according to the method used there. The data corroborate the immediate interaction of neurons in the cross-correlation analysis. The authors studied the cat motor cortex neurons with a tungsten electrode to keep intracellular recording. The stimulating current intensity was 2-2.5 times above the threshold values to induce a postsynaptic potential designated as mono- or polysynaptic on the strength of respective latencies—below or above 1.3 msec. The monosynaptic PSP region had its limit in space at 0.5 mm away from the stimulation site and the polysynaptic effect was observed within a 1.0 mm distance from the site. Barely one third of the investigated neurons showed a monosynaptic PSP. The authors carried out a series of experiments in which the stimulating electrode recorded multineuronal activity with large-, medium-, and small-amplitude spikes and the second electrode registered excitatory PSP (EPSP) of the neighbouring neuron. The analyser beam was triggered by separate spikes of a series picked out from multineuronal activity and accumulation was achieved by PSP delivered from the second electrode. Not all of the separated impulse series evoked PSP in the neighbouring cell. Of the 19 pairs of neurons eight pairs exhibited a correlation connexion, and all eight of which proved to be monosynaptic. The

neurons with polysynaptic connexions failed to show PSP correlation with extracellular spikes.

The above evidence describes the cross-correlation method as a potent tool in studying close-spaced neighbouring neurons. It lends weight to the assumption that monosynaptic connexions are functionally more effective than the influences exerted via polysynaptic pathways, and occur more frequently between neighbouring cells.

In Livanov's laboratory (Livanov, 1975) the relations between the impulse series of two neurons located in different projection areas of the cortex are used to define the periodicity of excitation in the cortical neurons. Spatially separated neurons activate one another with a periodicity of 2 to 5 Hz. Basing himself on the findings of cross-correlation analysis of impulse trains of two neurons, Livanov (1975) outlined a supposition about differentiated impulsion as he observed the dependence of a neuron's impulse upon one among a hundred impulses of another neuron. To put it differently, in a homogeneously manifested impulse train there were found pulses with varied functional significance in terms of propagation pathways. On that assumption, any impulse series generated by one nerve cell, especially a cortical cell, should be seen as an information set containing several complex-coded messages. The important deduction from this is that, when we analyse the activity of a nerve cell by different parameters of impulse activity, we every time actually recover from the impulse train messages of different content. Then it is correct to consider as truly network neuronal properties those which are displayed in the process of studying interneuronal relations.

The results obtained from the correlation of cross-interval histograms with quantitative parameters of an individual cell such as mean impulsion rate, post-stimulus histograms (PSH), and interval histogram (IH) have shown that not only does the cross-analytical method offer an objective portrayal of the organization of neuronal microcircuitry, but it also gives an idea about qualitative properties of systemic neuronal activity. Studies by Griffith and Horn (1963), Wyman (1966), Perkel et al. (1967) and other authors contain data to the effect that the nature of the activity coming from an individual nerve cell does not correlate with the indices of neuronal statistical connexions and does not control interneuronal relations by cross-correlation analysis.

Work by Rapoport and Silkis from our laboratory has provided new data on the correlation of cross-interval histograms with the autocorrelograms of cortical cells in the visual cortex of a cat. The types of the interneuronal connexions showed no dependence on the distribution pattern of the interimpulse intervals. The same form of dependent relations between two neurons could be observed for different types of autocorrelograms.



We have already seen that the statistical method, by virtue of being an indirect method of research on interneuronal relations, requires further evidence to substantiate its physiological importance. The direct way of analysing the functional connexions between neurons would call for recording of the postsynaptic potentials through one electrode tapping into the cell.

We have managed to find the only study investigating the functional connexion of neurons in the neocortex with reliance on intracellular characteristics. Raabe (1974) described the relationship between postsynaptic potentials in the motor cortex of anaesthetized cats. Her equipment featured a double-barrelled glass microelectrode with a tip spacing of 80  $\mu\text{m}$ . Overall, three pairs of neurons were investigated and in none of them was there any traceable connexion between the action potential of one neuron and the postsynaptic potential of another neuron. Stimulation of thalamic nuclei (specific and non-specific) induced either simultaneous or independent hyperpolarization in the neuronal pairs investigated.

Some studies examined functional connexions according to the correlation between extracellular spikes and postsynaptic potentials. Mendell and Henneman (1971) studied the dependence of motoneuronal EPSP on the impulses induced in a single fibre of the dorsal root in cats. One fibre has thus been found to send out terminals to 300 motoneurons and one motoneuron to be connected with 60 fibres. Jankowska and Roberts (1972) used this method to identify a relationship between an inhibitory interneuron and a motoneuron in the cat spinal cord. They activated the interneurons by ionophoretic glutamate application while keeping an ongoing record of the postsynaptic potentials of the motoneuron from each of the spikes produced in the interneuron. A unitary monosynaptic IPSP would appear in those motoneurons whose distinctive characteristic was a disynaptic IPSP due to the activation of Ia afferents.

Most probably, the direct intracellular investigation of interneuronal relations potentially goes beyond the data outlined in the foregoing. There is no doubt, however, that such studies are fewer in number than those concerned with the cross-correlation analysis of two impulse trains. The reason for the limited applicability of the intracellular method should be sought in the technical complexities besetting such experiments. What seems to us essential is that the method of direct analysis renders neuron activity and the dynamics of plastic readjustments in neuronal interaction closed to long-term observation.

To generalize on the data available in the literature with regard to multineuronal activity and cross-correlation analysis, both can be justifiably regarded as adequate and meaningful approaches

that offer key insights into the structural and functional organization of the cortical microcircuits. As a physiological concept, the neuronal circuit is currently in the process of change from its former realm of theoretical and model conceptions to a novel area where it is going to be studied experimentally and its functional properties quantized.

Hitherto discussion has centred on the mathematical procedures to explore interneuronal connexions and the criteria guiding physiological interpretation of statistical data. But, unless supported by additional information about the morphology and localization of the two neurons whose functional relations are being established, statistical computations are to some extent isolated. Supposing two motor-cortex neurons have been identified and the cross-correlations between them investigated but with no data available on their types and spatial interrelations. What are the messages it conveys, physiologically? There is only one, and it tells whether there is a functional connection between them. To this one may add some idea about the character or type of the connexion, if there is any, and go on to specify it as excitatory or inhibitory. For all that, any speculation on the functional organization of the neurons in a cortical projection area or a neuronal microsystem will be groundless and unconvincing. In itself, the neuronal pair represents the minimal number of elements sufficient to judge only the validity of using statistical techniques for the analysis of the system (interconnected) activity of neurons but insufficient for the description of a structurally delineated group of neurons.

There are studies in the literature addressed to interrelations among three neurons or more (Gerstein, 1970; Gerstein, et al., 1978). The studies, however, have relied on models and computer-based techniques. In physiological experiment, research on the forms of cortical neuron integration in a microsystem seems distinctly possible in conditions of multineuron registration that lends itself to the isolation of at least three impulse trains, each identified by morphophysiological properties of neurons. By morphophysiological properties we mean neuron size and parametric properties: mean frequency, responsive capacity, and distribution of intervals.

In the field studying the activity of cortical neurons on the basis of multineuronal recording data there are two distinctive approaches to the analysis of functional connexions. One of these concentrates on the types of connexions, classifying them into excitatory, inhibitory and composite. A second approach seeks to describe separated neurons morphologically and categorizes them on the basis of spike amplitudes with the classes of large-, medium-, and small-size neurons.

The statistical analysis of functional connexions among the three classes of neurons reveals their network properties, the properties of cells recognized by amplitude or size that are important

for an understanding of their synaptic organization. The network properties are construed here as including the ratio and quantity of inputs and outputs of individual neurons in a three-neuron system, which allows the state of four connexions to be described for each element of the microsystem. Of the four connexions, two relate to the input and the other two to the output forms of impulse influences.

Research findings on background activity in alert cats show differentiated and characteristic network properties for every class of cortical neuron. Irregardless of what particular projection area was observed, all small neurons experienced influences exerted by their neighbouring neurons. In other words, their inputs exhibited superior activity relative to the outputs. In any case, this was the picture obtained in the sensomotor, visual, and auditory cortex in the cats maintained in the alert state.

Larger-size neurons, those

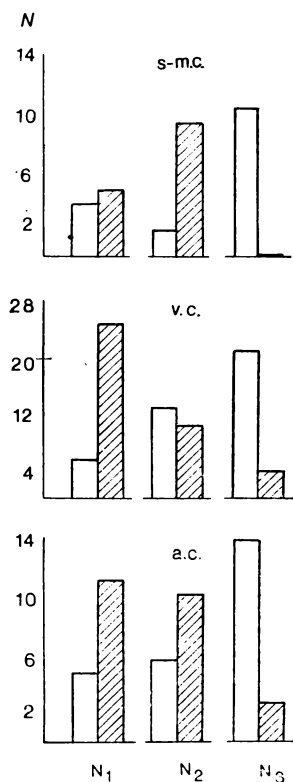


Fig. 3.6. Input-output correlation of functional connexions in neurons at different projection zones of the neocortex.

s.m.c.—sensomotor cortex, v.c.—visual cortex, a.c.—auditory cortex; N<sub>1</sub>, N<sub>2</sub> and N<sub>3</sub> are large-, medium-, and small-size neurons respectively. Open columns denote input connexions (to the neuron) and hatched columns identify output connexions (from the neuron).

of large and medium amplitude, mostly revealed the inverse pattern of relationships so that their output activity had an advantage over the inputs. At the same time, the network properties of the large and medium neurons indicated their distinctive ways of functioning in the microsystems of various projection zones. And, just as

the medium-size neurons displayed similar network properties in the auditory and sensomotor cortex, so too in the large neurons the similarity was quite obvious in the visual and auditory cortex (Fig. 3.6).

Considering these data, it seems likely that the neurons of different classes participate differently in the organization of the integrative activity of the respective projection zones, though afferent stimulations may be responded to in a like manner by all of them in terms of type and latency of the response. The point must be re-emphasized here that the network properties of neurons which depend on their functional relations are unpredictable from data on their individual (parametric) characteristics such as mean rate of impulsion or poststimulus and interval histograms.

A detailed analysis of neurons' association into a microsystem in terms of types and directions of connexions brings to light such a complex picture of neuronal interrelations as to demand a special discussion. But in order to obtain a general notion about possible forms of neuronal organization in the cortical areas, it suffices to deal with the distinctive features of connexions within and between microsystems which come into focus in a statistical investigation of multineuronal activity.

A comparison of connexions between neurons irrespective of their size differentiation draws attention first of all to the significant fact that neuronal interactions are more evident in the cortical microplots with neuronal disposition in groups, than with their location in different microplots (Fig. 3.7). Such a multidirectional and intensive form of connexions in the neuronal microsystem persists and moreover intensifies with the development of conditioned activity. If examined in isolation, the microsystem could be seen to have a certain tendency in the pattern of change of the interneuronal connexions. As reflex elaboration and consolidation proceed, the connexions become increasingly strong at the expense of the influences of the excitatory type. Even with an inhibitory conditioned reflex the tendency persists. But, oddly enough, the neuronal interconnexions between the microsystems are not enhanced, though they do undergo qualitative restructuring. With the inhibitory reflex, however, the interneuronal connexions that hold the microsystem together tend to decrease considerably.

The above data reveal only a very general and far from complete idea as to the possible form of integrative operation of cortical cells. They do provide, nonetheless, sufficient evidence for a number of conclusions based on the morphophysiological characteristics of multineuronal activity and the information available about the tri-neuronal type of representation for the activity of local neuronal groups.

First, in the microsystem of cortical neurons there exist functionally detached classes of neurons with differentiated network properties.

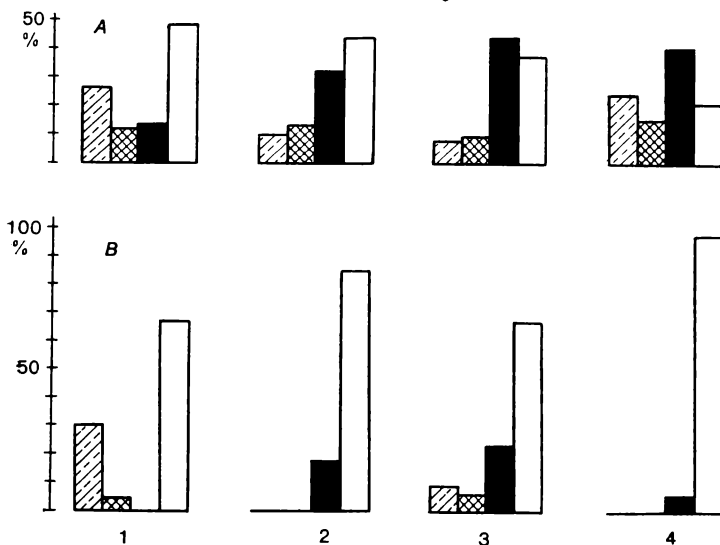


Fig. 3.7. Correlation of neuronal connexion types at different stages of motor reflex conditioning and extinction. Auditory cortex, chronically implanted electrodes. Clicks were combined with electrical skin stimulation, making an ongoing record of multineuronal activity and of the myogram of the stimulated paw in the cat.

A—types of connexions in the cortical microplot underlying one of the electrodes; B—types of connexions between neurons in different cortical microplots; 1—before pairings; 2—at the period of stimuli pairing until conditioned reflex has appeared and consolidated; 3—at the stage of consolidated conditioned reflexes; 4—at the stage of extincted conditioned reflex. Oblique hatching denotes inhibitory connexions, cross-hatching identifies composite inhibitory-excitatory connexions, dark columns designate excitatory connexions, and open columns designate the lack of connexions.

Second, neurons in a microsystem are more tightly connected than neurons in different microsystems.

Third, any functional connexions among cortical neurons are subject to plastic readjustments.

The last two conclusions may be of use in drawing up a possible scheme for the propagation of impulse trains through cortical cells.

From the experimental data such a scheme would depict excitation as capturing areas in the neocortex with some delay at the latter's microplots, and not uniformly. With respect to the specific spreading pattern of afferent excitation, the involvement of neurons in the activity must be shown in the scheme as saltatory and proceeding by leaps from one microsystem to the next. It is as

though every microsystem served as a trap of sorts for the excitation, in which the latter were to be driven through filtration, owing to the different-type reciprocal connexions present (Batuev and Pirogov, 1979).

In any 'neuronal trap' information processing takes time, the time factor depending presumably on the effective functional connexions among the neurons in the microsystem. The latter were shown earlier to be formed as adaptive reactions develop.

The neuronal microsystem has been used as an example to demonstrate the specific character of possible circuits of interneuronal connexions and their dissimilar developmental patterns under different conditions of exposure influencing the nervous system (Gassanov et al., 1979). The specificity of the interneuronal organization may be seen as a neurophysiological expression of the processes bound up with the analysis of a stimulus for its signal properties. From such a viewpoint the microsystem constitutes a functional unit and the locus of an elementary analysis of the stimuli as to their biological implications. Probably, the complexity of the system or interconnected activity of a microsystem is a constraint on the time of the analysis in it. As concerns the connexions between microsystems, their investigation has as yet been limited in scope. A comparative study of such connexions in the auditory and motor areas of the neocortex in the cat was accomplished by Galashina and Bogdanov in our laboratory. They showed that, in the motor cortex, the connexions become detectable over longer distances than they do in the auditory cortex. Furthermore, the statistical indices of the dependent relations were often found to have the same character as in a single microsystem taken in isolation. The short temporal parameters disallow the supposition of any sequence in which microsystems join in their integrative operation, though differences in the time course of the microsystems activation have been observed in some instances.

In this context, the research results are interesting that are devoted to connexions between neurons located at different areas of the neocortex (Zhadin et al., 1973; Livanov, 1975; Merzhanova, 1979). In the statistical analysis of the interrelations between spatially removed neurons, the correlation indices appeared at large time intervals in the order of tens of milliseconds. One of the explanations for the delays may be seen in the existence of the 'neuronal traps'. It could be that the spread of excitation from one cortical zone to another progresses with delays in the microsystems, needed for the recognition and collation of signals.

Many of the questions bearing on the theory and recording methods of multineuronal activity still need to be explored and elaborated in future studies. Nonetheless, enough experimental material has been accumulated to date to feel reasonably certain of the

potency of the analysis of multineuronal activity as an effective tool of research in neurophysiology—a discipline which hitherto has been burdened with generalities like network, system, and integrative activity.

Experience shows that multineuronal activity and the appropriate mathematical procedures for its analysis create between them a solid foundation for the understanding of the physiological principles of neuronal integration. It likewise suggests that 'system' and 'system activity' become meaningful concepts with realistic and objective connotations.

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## Adaptivity and Dynamic Properties of Visual Cortex Neurons

*I. A. Shevelev, D.Sc. (Biol.)*

Major advances in research into visual cortex neurons as detectors (Hubel and Wiesel, 1962, 1965; see the review: Stone and Freeman, 1973; Shevelev, 1976; Supin, 1974) tuned on definite line orientations and directions of stimulus movement and its spatial frequency have brought forth the now widespread perception of the neurons' significant rigidity and operation precision as well as invariance of their performance as detectors. There has been an increasing body of evidence over the recent years, suggesting high flexibility and plasticity in the properties of visual cortex neurons, and not only in early ontogenesis, but also in the adult animal. These data properly refer to the variation of the cells' receptive fields (RFs) with different levels of visual adaptation (Sasaki et al., 1971; Shevelev et al., 1974, 1977; Shevelev, 1976; Shevelev and Maximova, 1979; Shevelev and Verderevskaya, 1979), change in the level of alertness (Robertson, 1965; Verderevskaya, 1978; Shevelev and Verderevskaya, 1979) and contrast between stimulus and background (Shevelev et al., 1980).

We mean that many factors modify not the maximal ('morphological') receptive field of a neuron limited by the sum of all receptors with a potential capacity to send their signals to it via the intermediate level cells. It should be pointed out that under different conditions we reveal one of the neuron's multiple 'functional' RFs that occur within the maximal RF (Shevelev et al., 1974, 1980). An important reservation is that the flexibility and plasticity of the cortical neurons are taken to mean here as fast-working commutations of connexions responsible for RF functional reorganization (Bullok et al. 1977), and not just their comparatively slow readjustments, brought about by learning or training.

The understanding of the flexibility, plasticity and dynamic properties of cortical neurons underlying the mechanisms of adaptivity is of prime importance also in elucidating the mechanisms of conditioning which involve, as an essential element, modification of the neurons' properties and connexions in the cortical projection of the conditioned stimulus.

The specific aim of the present paper is to summarize our data about considerable adaptivity of the cat's visual cortex neurons and their tuning to changing tasks solved by the animal's vi-

sual system and organism in various conditions. It seems appropriate to cite here also some data on the dynamics of neuronal properties during the period of response development. Finally, data on the psychophysics of human visual perception are included here as a necessary input for the assessment of the behavioural significance of the neuronal properties being studied.

#### 4.1. METHODS

The neuronal part of the present study was accomplished in acute experiments on adult cats immobilized with 0.15 ml/kg of d-tubocurarine in a 10 per cent solution. The animals received no general anaesthesia and had the sites of incisions and painful points on the head thoroughly infiltrated with a long-acting anaesthetic (0.5 per cent celnovocain). They were intubated and changed to artificial respiration, their rectal temperature kept constant (38°C) throughout the experiment by means of an ultrathermostat. The state of the brain and the level of alertness were monitored by EEG. The third eyelid was removed and the eyelids opened; a contact lens was put on one eye, the pupil was dilated with an 0.1 per cent atropine solution, and the second eye was covered with an opaque partition.

The skull was trephined over the primary projection region of the visual cortex (area 17): P-0.5; L-0.5 ÷ 2 mm, or, in some of the experiments, over the posterotemporal gyrus (area 21): P-1.0; L-12.0 mm. In control experiments on lateral geniculate body neurons (LGB) electrodes were inserted to the point with the coordinates: A-7.5; L-10.0, H-12.5 mm (over 'Horsley-Clarke's O'). The cat's head was rigidly fixed in an CTM-3 stereotaxic apparatus and the coordinates were determined from the Jasper and Ajmon-Marzan atlas. In some of the control experiments the head was fixed with a metal platform attached to the skull by duracryl, whereon the manipulator with the electrode was mounted in that case. In most experiments an CTM-3 microdrive was employed for micro-electrode penetration at 5 µm steps.

The microelectrodes were either glass, filled by 2.5 M NaCl solution with the resistance of 5 to 15 mΩ at the frequency of 60 Hz, or acetate-coated tungsten with the resistance of 1 to 5 M. Through a cathode follower and amplifier of the 'Biophas-IV-2-4' oscilloscope (Alvar, France) extracellularly recorded impulses were fed to a threshold former. Standard impulses were given on-line into a KVT-250M analyser (SAIP, France), or modulated the beam of an RF's express map recorder (Meshcheryakov et al., 1977).

In some experiments the impulses were fed into an IN-90 mini-computer (Interthechnique, France) for a more elaborate processing (see below). The common procedure was to store PST-histo-

grams of neuronal activity (from 20 to 30 realizations) in the analyser or computer. They were used to estimate the average number of impulses and their maximal frequency in a particular burst or in the total neuronal response, as well as in estimation of temporal reaction parameters, such as the initial and peak latencies of every burst and the time of its cessation.

The experiments were carried out in a light- and sound-proof screened chamber at three levels of visual adaptation, namely photopic (3-10 lx on a white reflecting screen with the reflectance of 0.95), mesopic (0.01-0.1 lx), and low scotopic (practically dark). The needed screen illumination was provided by a separate light source with a stabilized controlled feeding. The light stimuli, in the form of local light bars of variable size, orientation and localization in the visual field, were presented monocularly on a white reflecting screen 60×60 degr. in angular dimension. Their intensity and contrast with the background were controlled over a wide range (60 dB), using calibrated neutral glass density filters with a step of 2 dB or greater. In some cases, a polaroid optical wedge was used for more precise adjustment of the stimulus contrast against a changing background. The exposition varied in duration from 10 to 1000 msec. Also, images with different trajectories of movement and speeds (0.5 to 50°/sec) were used and, to assess the neuron's directionality, different-size spots were moved about in various directions through the RF centre. In express mapping the light bar scanned a pre-selected area on the screen. In the latter case, the beam of the recording oscilloscope traced out the same trajectory, its brightness modulated by neuronal discharges (Meshcheryakov, 1977). The duration of the scanning operation, i.e. recording of an RF's express-map, would usually range from two to three minutes, depending on the scanning speed and scale.

In computer-controlled experiments, the position of the stimulus on the screen, the trajectory and speed of its movement, and the exposition were set in conformity with one of the programmes which the computer selected and parameterized according to the pre-assessed properties of the neuron RF and the experimenter's instructions. The hardware in all experiments included a universal photostimulator (Shevelev et al., 1976) with a two-coordinate mirror galvanometric system and an electronic shutter. The stimulator was driven by two low-frequency function generators (Г-6-15 and ГПНК-3) and a Physiovar electronic stimulator (Alvar, France); in the computer-controlled experiments this was done by the IN-90 minicomputer (Interthechnique, France) through a specially designed controller\*.

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\* The author acknowledges with gratitude G. A. Sharaev and M. F. Pyshny who developed the controller and the programme package for the controlled experiment.

For a part of the experiments, the information obtained was stored on magnetic tape (an SDR-41 recorder, Nihon Kohden, Japan) and then fed into the computer for processing. The RF express maps were recorded on photographic film. The outputs of computer processing were stored on floppy discs and magnetic tape and printed out with a high-speed alphanumeric or x-y plotter.

At the onset and end of each experiment and, if necessary, many times in-between, projection ophthalmoscopy (Fernald and Chase, 1971) was applied to correlate the retinal and screen coordinates and determine the optical power of the correcting lens which was then mounted in front of the contact lens. In several experiments the horizontal EOG component was recorded to allow the assessment of possible residual eye movements.

In total, the present work has absorbed data of 230 experiments obtained in detailed studies of 563 single units in area 17 of the visual cortex, contralateral to the stimulated eye, and of 103 units in area 21. The length of neuronal activity recording varied from tens of minutes to 4-5 hours. The work with each cell began with a qualitative appraisal of key characteristics of its RF in a light adaptation conditions, i.e. the size, shape, orientation and localization in the visual field, preferred velocity and stimulus direction of movement. With this as a basis and with account taken of the frequency of background discharges and the acuity of detector tuning, RFs were classified according to their degree of complexity (Hubel and Wiesel, 1962, 1965). Following the preliminary qualitative appraisal of the neurons' properties, a detailed quantitative analysis was performed on the latter's characteristics.

In psychophysical experiments on adult healthy subjects we tried, as much as possible, to adhere to the same light stimulation schedules as in the neurophysiological experiments on cats. This involved using either the same universal photostimulator or a three-channel tachistoscope to study the influence of various factors on the parameters of recognition by human subjects of the shape, orientation or size of the visual stimulus.

## 4.2. RESULTS

### *1. Adaptational changes of visual cortex neuron RFs.*

Mapping the RFs of neurons in the primary projection region of the visual cortex (area 17) under various adaptation conditions showed the RFs to go through a major reconstruction in the overwhelming majority of the instances. When passing from the photopic to mesopic light adaptation environment, in almost 70 per cent of the neurons, their RFs underwent, within tens of seconds, a certain expansion; their shape became more simple, changed from elongated to circular or elliptical, and the acuity of orientational and directional tuning of the neuron in question was reduced (Fig. 4.1).

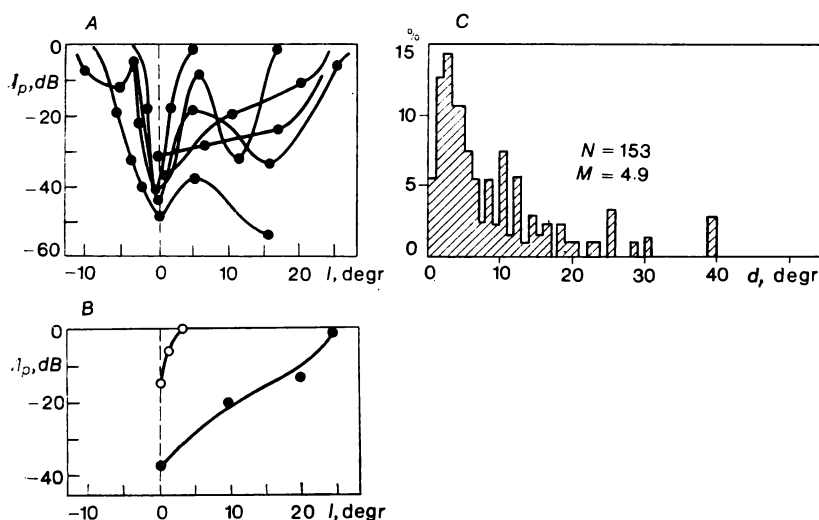
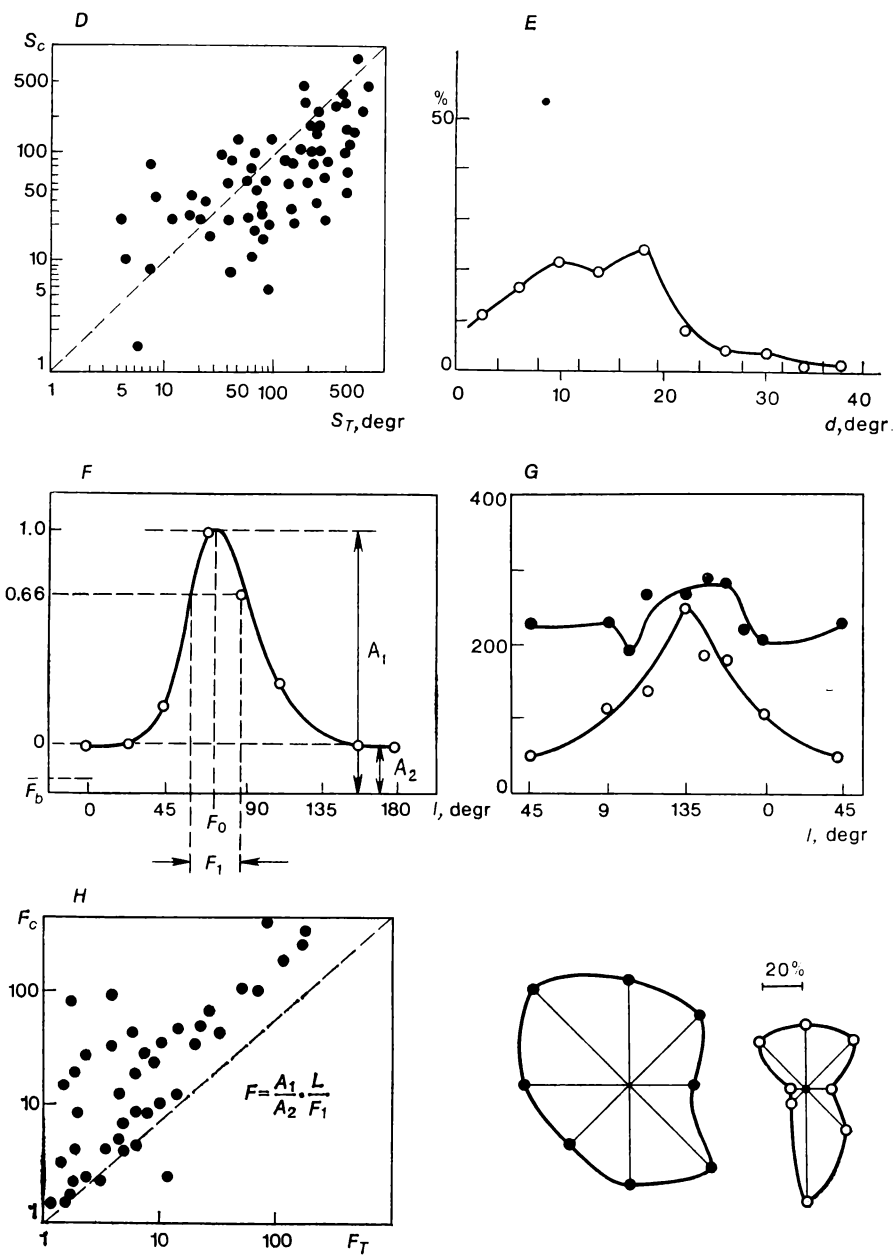


Fig. 4.1. Adaptational changes of the receptive fields (RFs) and detector characteristics of neurons in the cat visual cortex.

A—threshold excitability reliefs of several neurons, the abscissa—distance from the RF centre in degrees, the ordinate—threshold of the neuronal reaction to local stimulation in dB of attenuation of maximum light intensity, taken as 0 dB. Dark adaptation; B—same as in A for one neuron in a dark (black dots) and light (white dots) adaptation; C—distribution of neurons according to maximum RF dimension in conditions of light adaptation. The abscissa—RF diameter in degrees, the ordinate—percent of neurons to the total number of studied neurons; D—same as in C, in conditions of dark adaptation. Each point designates data for one neuron. The equality of RF areas in the two conditions is shown by a broken line; E—measurement of the characteristics of orientation tuning of the neuron. The abscissa—turning angle of the light bar flashing in RF, in degrees; the horizontal orientation of the slit is taken as 0° and the vertical as 90°, ordinate—relative frequency of neuronal discharges;  $F_b$ —the level of background activity, 0—response to non-preferred and 1.0 to preferred orientation,  $F_0$ —preferred orientation,  $F_1$ —width of orientational characteristics by the 0.66 level; G—example of change in orientational tuning of the neuron when passing from light (white dots) to dark (black dots) adaptation. The axes are the same as in F (the ordinate is in imp/s); H—change of the total characteristic of orientational tuning when passing from dark (abscissa) to light (ordinate) adaptation. Each point designates data for one neuron. Marked improvement of orientation detection parameters in light is clearly evident; I—distribution of recorded neurons (by preferred directions of stimulus movement in dark (on the left) and light (on the right) adaptation. Plotted on the axes is probability of detection in a cell population of a specific preferred directionality.



It should be pointed out that under the same conditions nearly one fifth of the cells under study exhibited directly opposite changes of RFs and detector properties, and only 10 per cent of the neurons did not rearrange their RFs in any significant manner. Experiments with equal contrast between stimulus and background revealed that the adaptational RF readjustments described above did not disappear after the contrast equation, that is, were not determined by this factor.

Further diminution of the adaptation background from the mesopic to the extremely low scotopic level (actually to darkness) caused neither additional RF expansion, nor the reduction of detection acuity in most of the cases. Conversely, in some of the cases the RFs even narrowed down slightly, still more often remained unchanged.

It is important to note that not only the detector characteristics of each cell, but also the capacity of the whole population to abstract certain parameters of the signal at the day-light level of illumination improved substantially and the population was specialized as it were (Fig. 4.1, *I*).

An important point associated with the use of light stimuli at a low adaptation background is one of light scatter in the eye media. Potentially, it can imitate the effect of RF enlargement due to neuron stimulation with diffuse light reaching its RF in stimulation of remote points in the visual field.

Drawing on the data about the light-scattering gradient in the cat retina (Robson and Enroth-Cugell, 1978) and our own measurements of the gradient of light scattering over a screen, caused by imperfection of the stimulator optics, we have been able to see in what instances these factors could lead to an artifact 'seeming' expansion of the RF threshold reliefs. It turned out that in the majority of cases diffuse light of near-threshold intensity, delivered to the RF surround, had been too weak to elicit a supra-threshold or threshold reaction of the neuron through its action on the RF centre (Shevelev, 1980). An important testimony against the decisive role of diffuse light in RF enhancement in the low background condition lies in the fact that the mesopic background, as distinct from the dark one, fails to set off a major RF readjustment, though the relative role of diffuse light falls dramatically. It should be recalled also that in some of the cases we obtained adaptational RF changes opposite to the typical ones—those directed against the influence of diffuse light. In a minor group of neurons the adaptational RF changes did not become manifest at all. All this leads us to believe that the aforementioned data do reflect faithfully the considerable adaptational variability of neuron RFs in the cat visual cortex, though the prevalent view to date has asserted the presence of such properties in the retinal and LGB neurons alone.



*II. Animals' alertness level and the RFs of visual cortex neurons.* We thought it important to find out whether the input systems of visual cortex neurons were subject to readjustments in other conditions than the purely visual adaptation situation. To put it differently, the question was: are there any other drives to the intracortical mechanisms for these neurons' RF modulation? To answer the question, experiments were performed at varying levels of alertness in the animals.

In order to increase the alertness relative to the control, we relied on a weak tactile stimulus—an air-puff at the corner of the occluded eye (not used for light stimulation). In humans, this results in feeble eye contraction and a slight unpleasant sensation. Immediately after the air-puff exposure a series of RF express-maps of the cat neuron were recorded to permit defining the dynamics of RF post-exposure changes, compared to the control measurements.

In some instances, spontaneous RF changes unrelated to any controlled impacts, were also recorded with a view to gauging variability of the control estimates. As a rule, these changes did not exceed 10 to 15 per cent of the RF area.

Following the air-puffs, we found distinct and lawful (repeated) RF changes in a great majority of the cases. Varied in duration from 15 to 30 minutes, the changes would most frequently involve reduction of the excitatory centres and extension of the inhibitory surround (Fig. 4.2). Much less frequently (21 per cent of the cases) the RF changes came through with the opposite sign or not at all (5 per cent of the cases). Significantly, all these RF rearrangements with the increasing alertness level could be clearly seen at all three visual adaptation levels—dark, mesopic and photopic. In response to the airpuffs the RF length (the greater dimension) varied most and the RF width (the smaller dimension) somewhat less. It is worth noting that in some of the cases (29.1 per cent) the greater and smaller RF dimensions changed post-exposure in opposite directions or one of them changed and the other did not (22.7 per cent).

In order to produce an opposite effect, that is, to reduce the alertness level in an animal we applied intravenous injection of the narcotic drug sombrevin at a low (1.5 mg/kg) dose which induces in humans only a brief (several minutes) loss of consciousness. It was found that in 57 per cent of the units with excitatory RF centres this had been followed by the latter's expansion lasting 5 to 30 minutes. In the rest of the neurons of the same type the RF centres contracted for some 20 to 30 minutes. The inhibitory RF centres would most typically increase in area (67 per cent) though in one third of the cases their area decreased. As regards inhibitory

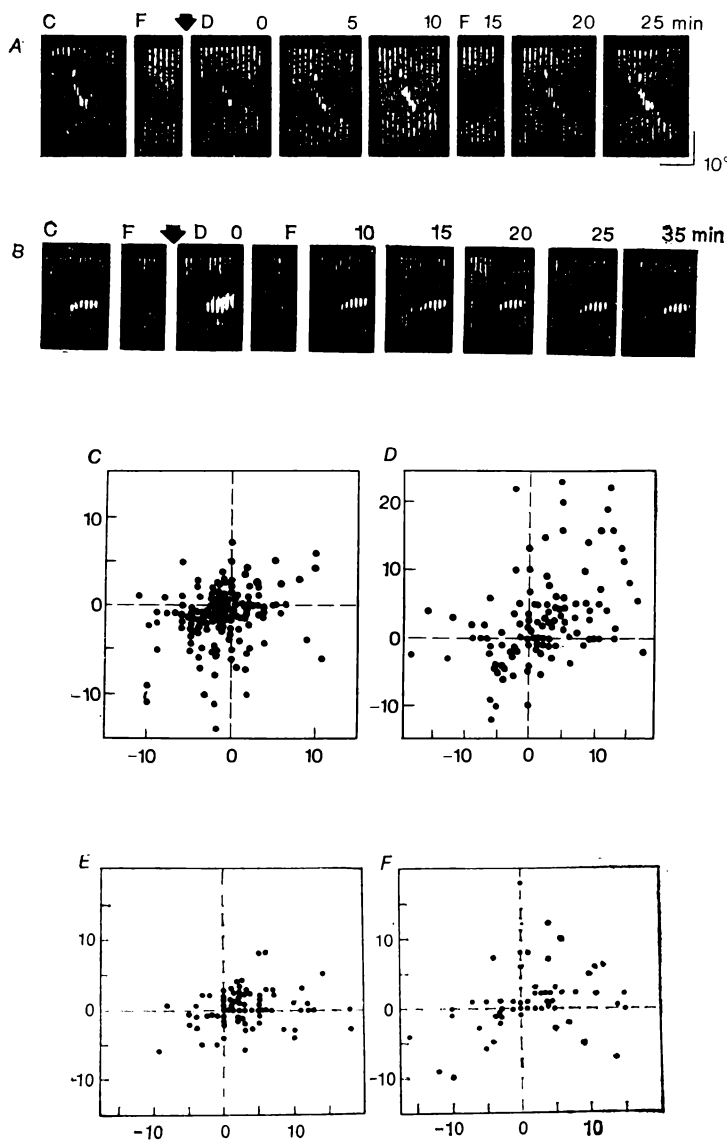


Fig. 4.2. Changes of RFs of visual cortex neurons with a changing level of animal's alertness.

A—examples of RF express-maps of one of the neurons in a quiet state of the animal (C) and at different time intervals (figures in minutes over the maps) after the exposure to a weak tactile stimulus (air-puff, D) increasing the level of alertness; F—background activity. Calibration of RF—10°; B—same as in A for another neuron, after the action of a light narcotic drug, somnolevin; C—changes of RF horizontal (abscissa) and vertical (ordinate) dimensions after enhancement of the alertness level. Data for RF excitatory centres. Taken as 0 are control RF dimensions in degrees; D—same as in B, but for RF inhibitory areas (more often, RF surround); E and F are same as in C and D (respectively), but after reduction of the alertness level by injection of somnolevin.

RF surrounds with an excitatory centre, they alternately widened and narrowed in almost equal proportions (Fig. 4.2, *B, E, F*).

To sum up the results derived in this part of the study, one may well state, as a first approximation, opposite RF alterations with increasing and decreasing alertness levels of the preparation, as the RF excitatory centres mostly shrank in the former and extended in the latter case. It is noteworthy that the opposite, RF changes were frequently observed when studying the same neuron in both these situations (the air-puff and narcosis). Thus a variation of the alertness level produced changes in RFs of visual cortex neurons essentially similar to their adaptational readjustments in that the elevation of the alertness level (and an increase in the background illumination) resulted in RF narrowing in most of the cells, whereas the reduction of the alertness level (and also a decrease in the level of visual adaptation) induced the opposite effect.

*III. Characteristics of RFs of posterotemporal cortex neurons in the cat.* It was thought of interest to compare the RF properties of the neurons in area 17 with their counterparts in area 21 (the posterotemporal cortex) both with regard to their adaptivity and several other characteristics as well. As is known, area 21 has visual inputs but beyond that is closely connected to other (auditory, in particular) systems (Artemenko and Mammonets, 1972; Manasyan and Shevelev, 1981). Neuronal RF mapping in this area has revealed them to be similar in a number of ways to the cells in area 17, but also to have several basic distinctions.

The RFs in the posterotemporal cortex varied broadly in size and shape; some of them were of the rhomboid shape previously unobserved in the primary projection region. In average size, these RFs were much greater than those in area 17 at light adaptation but were likewise dependent on RF eccentricity in the visual field. It is very important that in the majority of instances (88 per cent) the area 21 RFs did not change, that is, had been invariant to the level of visual adaptation. It should be remembered that in area 17, conversely, 90 per cent of the units exhibited significant adaptational modulation of their RFs.

A distinctive feature of the neurons in area 21 stemmed from great variability of their RFs in the absence of controlled experimental impacts or EEG-revealed changes in the state of the brain. The effect showed itself as alternate appearance and disappearance of the neuron's responses within its RF, which was why the recorded field seemed to vanish for a few tens of minutes and then to reappear. What appears to be most interesting and functionally significant is that 14 per cent of the neurons in that area showed a shift of localization, in the visual field, of the RF recorded on the express-map. Such shifts were most thoroughly verified to make

sure that they had been caused by neither residual eye movements nor the drift of the mirrors in the stimulating apparatus. As will be seen in Fig. 4.3, *D* the distribution pattern of the amplitudes of

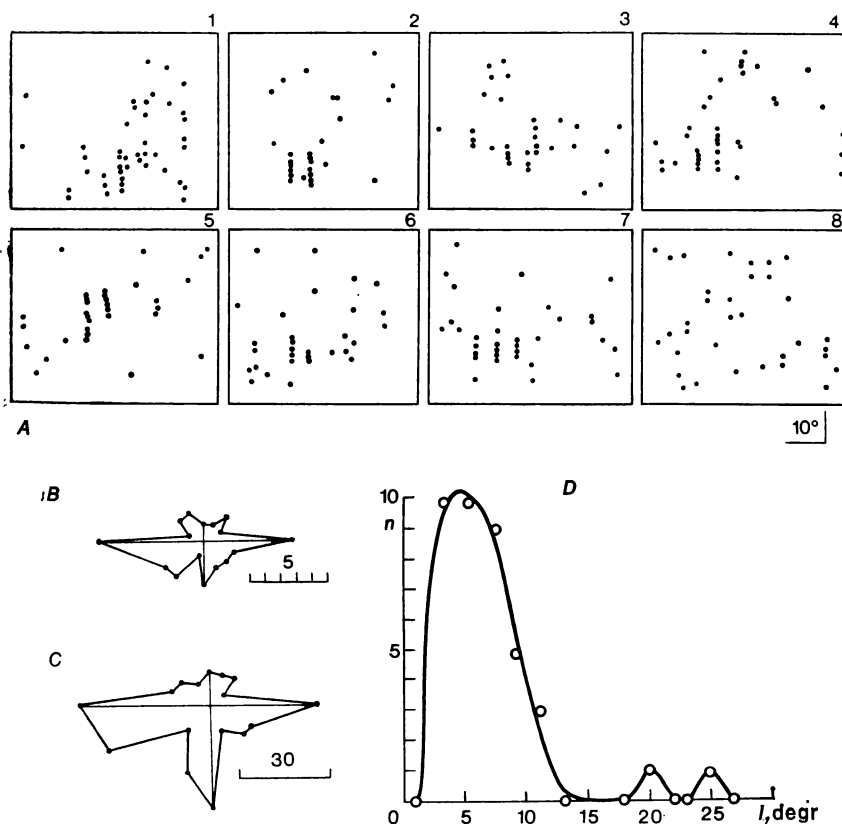


Fig. 4.3. Changes in the localization, in the visual field, of the neuron's RFs of the cat posterotemporal cortex (area 21).

*A*—express maps of the RF of one neuron taken at successive moments at intervals of several minutes. A shift of the area of excitatory responses in the tested part of the visual field is clearly seen; *B*—distribution of studied RF shifts by directions. Calibration—number of RF shifts; *C*—same as in *B*, but with account taken of the amplitude of shifts (calibration in degrees); *D*—distribution of studied RF shifts by magnitude (abscissa in degrees). Ordinate—the number of cases.

these shifts and the whole right-hand part of this distribution exceeds by far those 3° which the maximum shifts of the eye and the stimulating apparatus could achieve if they coincided in time and direction. Importantly, the RFs shifted largely in the horizontal direction (Fig. 4.3 *B, C*), this being in line with the dominant direc-

tion of eye movements in a non-relaxed cat. It looks quite intriguing to compare this effect with the action of the mechanism which ensures the constancy of visual perception when eye movements are on (of which more will be said in Discussion).

*IV. Dynamics of orientational tuning of cortical neurons in temporal microintervals.* Thus far we have discussed plastic adaptive readjustments of neuronal RFs in the visual cortex and extra-striate visual area which normally occur within seconds and tens of seconds but on occasion take tens of minutes. It seems obvious, however, that the readjustments of neuronal properties which come through within tens of milliseconds post-stimulation could be at least as important for brain activity.

These fast dynamic readjustments of the detector orientational tuning of cortical neurons were analysed with a method of time slices previously applied by Podvigin (1979) to the analysis of dynamics of LGB and retinal neurons' responses as a function of a circular light spot diameter. Under the method, a particular functional characteristic of a neuron is estimated not by a total number or maximal instantaneous frequency of impulses in a reaction, but by the frequency of discharges. Aided by the minicomputer, we obtained from a series of PST-histograms of responses to flashing light bars of different orientation stored up in the computer memory, a series of functional graphs that expressed neuronal activity frequency as a function of bar orientation in the first 20 msec after the stimulus, next 20 msec, and so on.

The experiments showed, in a major proportion (93 per cent) of visual cortex neurons, the lack of any stable orientational tuning in time. The most characteristic change took place in the acuity of orientational tuning, i.e. the width of the orientational characteristic at the level of 0.66 of its peak. In dynamics, this characteristic suggested a sharp orientational tuning in the first few moments of response development by the time the burst of impulses had achieved maximum development (an increase in the frequency of discharges), the tuning acuity deteriorated markedly to increase again towards the end of the response (Fig. 4.4, *A, B*).

On the other hand, two thirds of the neurons with their orientational tuning produced the phenomenon of scanning in a specific portion in the range of orientations. The effect comprised a gradually shifting maximum of the tuning curve in successive time slices, from some of the neuron's preferred orientations to other ones, thus seemingly scanning the range. In most of the neurons that displayed the effect, the preferred orientation moved clockwise and in one third counterclockwise. The scanning range varied from 15 to 112° (most often, from 45 to 60°) and scanning speed averaged  $1.25 \pm 0.3^\circ/\text{msec}$  (Fig. 4.4, *C-J*).

One would think that the discovered effects of dynamic instability and readjustability in the orientational tuning of the cat visual cortex neurons may be indicative, first, of the readjustment of the neurons' RFs in time microintervals where different RF areas apparently change asynchronously. Second, the data may suggest a basically new type of encoding information about the orientation of lines at the level of the orientation detectors in the primary visual cortex. In addition to the obvious place coding of the information, one should also assume the existence of a temporal pattern code as a means to ensure higher coding reliability as well as greater ease of information read-out from the screen structures of area 17 in order to relay it to the next parts of the visual system.

*V. Some psychophysiological parallels.* In the description and analysis of some new functional properties of individual brain neurons a question always arises as to the real functional and behavioural significance of the observed effects and regularities. Always one would like to take a further step to see if they amount to something more than a purely laboratory phenomenon and whether the

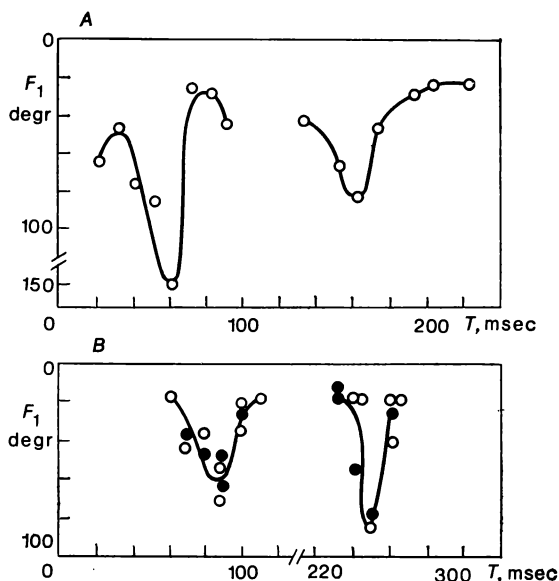
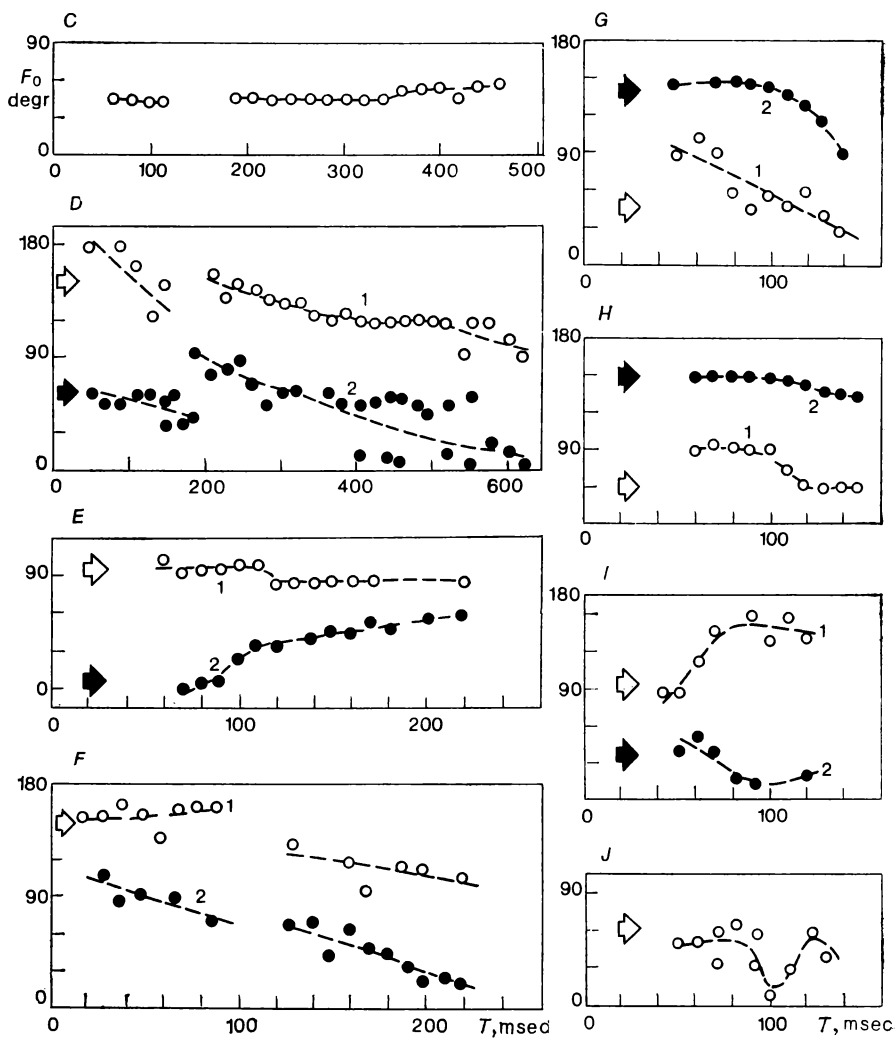


Fig. 4.4. Dynamics of orientational tuning of visual cortex neurons.

A—typical change of tuning width (ordinate in degrees,  $F_1$  is same as in Fig. 4.1,  $F$ ) with time (abscissa in msec). Curves on the right and left show the dynamics in the course of development of the first and second burst of impulses; B—same as in A for another neuron. 1 and 2—repeated control measurements; D-J—examples of preferred orientation dynamics (in degrees on the ordinate in all graphs) for various neurons. 1 and 2—the principal and second preferred orientations; C—example of stable tuning.



properties of neuronal structures revealed in neurophysiological experiments on single neurons manifest themselves in human behaviour and higher sensory functions.

With the object to answer this question, experiments were conducted in our laboratory attempting to study several characteristics

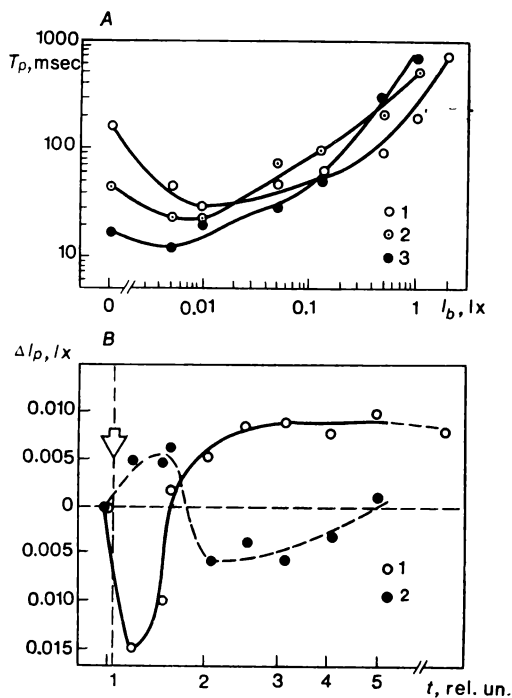


Fig. 4.5. Psychophysiological manifestations of adaptivity of visual-cortex neurons in experiments with human subjects.

A—dependence of the critical duration of presentation of geometric figures necessary for their recognition (the criterion is 0.75 correct responses) upon the intensity of adaptational background (abscissa in lx on the white) in successive experiments (1-3); B—dynamics of recognition (1) and detection (2) thresholds for a letter combined, in the first experiment, with finger pain stimulation (the arrow). Abscissa—time in relative units, log. scale (the last point—30 days). Ordinate—intensity thresholds in lx; plotted downward—the decrease, and upward the increase of the threshold relatively to the recognition and detection thresholds of two control (unreinforced) letters taken as 0.

of visual recognition in man by the criterion of his verbal response. Shown in Fig. 4.5, A are data (Kamenkovich, 1979) on the dependence of critical time of the tachistoscopic exposure of geometric figures on background illumination in a series of successive experiments. It can be seen that within the range of low background



illuminations the recognition time shortens with the growth of the background, a finding inconsistent with the pattern of contrast variation in that range. On the other hand, it is clear that training, or a progressively shorter recognition time from one experimental day to the next, occurs solely within the low illuminations (scotopic and mesopic) ranges. These developments may be revealing of the cortical nature of the effect and cortical RF readjustment in man with alteration of the adaptation background. Indeed, nothing but adaptational changes in the extent and intensity of RF detector orientational tuning can account for the reduced duration of recognition directed against contrast changes while the function's trainability points to the cortical nature of the effect.

Meshcheryakov (1977) found out conditioned dynamics for the parameters of recognition and detection of visible letters in man (Fig. 4.5, *B*). Upon reinforcement with a mild electrical shock a similar effect was obtained also using positive olfactory reinforcement of the image of one out of the three letters presented to a subject (with reinforcement applied only in the first experiment). The intensity threshold of recognition and detection of this letter, as opposed to the other two (control), changed significantly. During the initial 1.5 to 3 hours the recognition threshold declined appreciably (i.e. recognition improved) and then kept increasing for a long time afterwards (the effect was followed up to one month). The letter detection threshold, i.e. the subject's answer, 'I see the flash but don't know the letter', changed in dynamics conversely to the recognition threshold. Presumably, the observed effects give signs of long-lasting readjustment of the RFs of visual cortex neurons in man, triggered by backward conditioned connexions. If one assumes that the RFs of some neurons, selectively involved in the process of recognition of precisely the reinforced letter, readjusted themselves under such modulating influences (first contracted and then expanded for long), this could explain not only the dynamics of the recognition thresholds, but also the opposite changes of the detection thresholds. They should by definition behave reciprocally so that improved recognition in the contracted and sharpened RFs will unavoidably impair detection because of reduced spatial summation, and vice versa.

An attempt to control RF dynamic readjustments of visual cortex neurons and their detector operations in temporal microintervals was made by Kostelyanetz and Kamenkovich (1982). Using the tachistoscopic method of presenting different-oriented lines, they showed the probability of error in their recognition by man to increase significantly at exactly those moments after the onset of stimulation when orientational tuning acuity (see Section IV of the present paper) of the cat visual cortex falls off. There is every reason to assume that dynamic readjustment in the properties of vi-

sual cortex neurons in temporal microintervals is the cause of the psychophysiological effect observed.

*VI. Direct measurements of RF dynamics in microintervals of time.* We decided on the method of time slices for a study

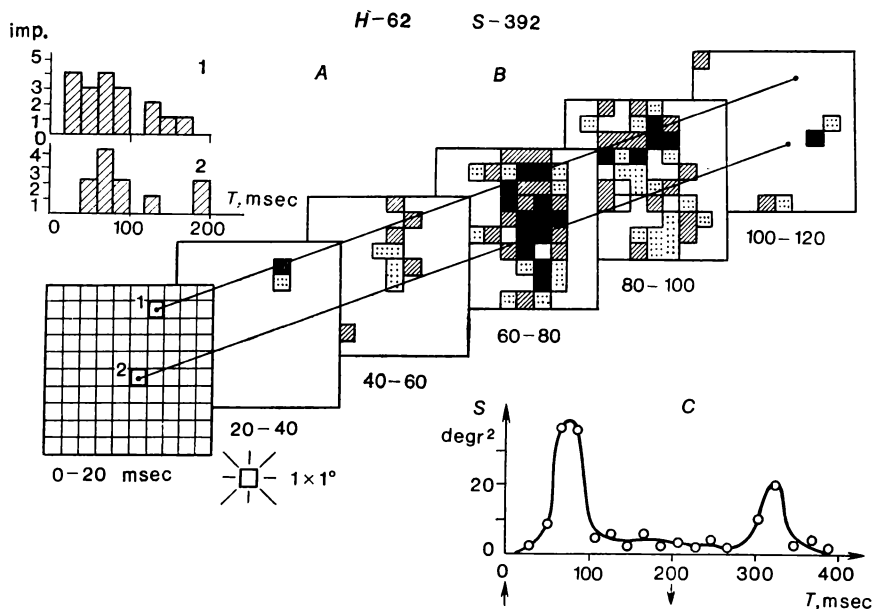


Fig. 4.6. Dynamics of RF excitatory area of the cat visual cortex neuron.

**A**—PST histograms of neuron's discharges in response to stimulation of its RF points 1 and 2 (see on the schematic 0-20 msec maps in **B**); **B**—a series of computer RF maps obtained by the method of time slices in a controlled experiment. The time of the slices in msec is indicated near the maps. Rate of blackening increases with the frequency of discharges. The flashing light stimulus is a  $1 \times 1^\circ$  square; **C**—the area of RF excitatory region of the same neuron (ordinate in degrees<sup>2</sup>) as a function of the time (abscissa in msec) after the start of the flash, its duration—200 msec. Stimulus on- and off-moments shown by arrows.

on RF dynamics of the visual cortex neuron. In a computer-controlled experiment the computer first scanned with a light bar the screen in front of a cat's eye and then, after exploring the area of responses, i.e. of the cell RF, to the movement of the stimulus, turned to its detailed, point-by-point exploration. To do so, a local light stimulus—a small light bar or square—was flashed at every one of the 100 RF points of a 10 by 10 matrix in a random sequence. In some measurement series the RF maps so obtained were also gauged for every neuron as a function of adaptation background and contrast as well as the stimulus intensity, size, orientation and length of presentation. With 100 PST-histograms

of the neuron's responses to the flashes at each of the tested points stored in the computer memory, the latter went on to plot by successive 20-millisecond parts of the histograms, a series of 20 RF maps that reflected the state of the field at successive moments in time.

It turned out (Fig. 4.6) that during the unit reaction all of the studied neurons in the visual cortex experienced regular and qualitatively rather similar dynamic changes. In the first 20 to 60 msec after the stimulus presentation the cell does not yet begin to respond (latency) and, consequently, the recorded RF of the neuron is not manifest at that time. But once the fastest-conducting parts of the unit inputs (in its RF centre, as a rule) begin to fire, a relatively small and centrally located zone of responses, or the recorded RF, makes appearance. The zone keeps expanding until reaching maximum and then begins to decrease due to the earlier termination of the reactions in the peripheral parts of the neuron's inputs. The last phase consists in disappearance of the responses all over the field, i.e. the disappearance of the recorded RF. If, however, the neuron were to generate a second burst after some time, the above process would recommence.

Similar dynamics of the RF excitatory zone was found also in off-responses of the same cell. Control experiments on LGB neurons demonstrated a principally similar development of RF dynamic readjustments there, too. The only difference involved somewhat faster progress of the RF dynamic phases outlined above and lesser RF elongation (in the LGB the RFs were more often circular or slightly elliptical).

Thus, measurements of the dynamics of the RF excitatory zone brought out direct evidence in support of the previously formulated propositions (see Section IV) about the existence of dynamic readjustments of RF zones that may be underlying dynamic changes of their detector orientational tuning.

#### 4.3. DISCUSSION

So, the findings of our experiments have revealed a set of facts in favour of considerable flexibility, plasticity, adaptivity and dynamic variability of the neuron RFs in the cat primary visual cortex and of detector characteristics of these cells. Psychophysiological correlates have been obtained, suggesting qualitative and quantitative similarity between behavioural manifestations of these effects in man and the alterations of neuronal properties investigated in electrophysiological experiments on cats.

These facts when analysed pose the question, first, about their neurophysiological mechanisms and, second, about their behavioural value for the organism and information-coding value for the

brain. Besides, it is worth considering probable points of conflict between the existing concepts about the organization of certain higher sensory functions and the ranging adaptive capabilities of visual cortex neurons revealed by us.

Earlier on (Shevelev et al., 1974; Shevelev, 1976; Shevelev et al., 1980), we have suggested that every visual cortex neuron possesses numerous adjustable RFs located within the morphological RF limited by all of its potentially existing inputs.

The assumption of broad variability and non-rigid fixation of these functional RFs in every neuron can alone explain the now multiplying data on considerable adaptivity and plasticity of the RFs and their detector functions. It should be added that such data are in dramatic conflict with the presently well-known and generally accepted hypothesis of Hubel and Wiesel (1962, 1965) which explains the mechanism of detector orientation specialization of these neurons by selective excitatory convergence on them of LGB afferents organized in a certain spatial order. The hypothesis leaves room neither for RF readjustments nor for their adaptational variability and plasticity in general.

Contrary to the idea, we have formulated a concept (Shevelev et al., 1974; Shevelev, 1976) of the mechanisms for the formation and adaptive modification of the specialized detector RFs of visual cortex neurons; it provides a simple and natural explanation for the whole body of data accumulated to date about their properties. According to our hypothesis, the excitatory convergence of cortical neurons is not specialized but diffuse and rather wide. As a result, in the dark adaptation environment, when the effect of intracortical inhibition is reduced or non-existent (due to the higher threshold of cortical inhibitory interneurons—see Shevelev and Marchenko, 1979), the cortical RFs become extended and their shape simplified (in fact, under these conditions most often large circular or slightly elliptical fields are encountered).

In accord with such RF structure and size, the cells' detector tuning shows significant crudity. On exposure to light or given increasing alertness levels, spatially specialized cortical interneurons become actively involved, inhibiting signals from the lateral RF parts and thereby causing considerable RF reduction and specialization. This makes the neuron a highly selective spatial filter of the signal properties (orientation, direction, etc.). Thus the radical difference between this idea and the traditional views concerning RF structure consists in attributing the formative function of the RF and its modification to the intracortical inhibitory mechanisms, and not to selective excitatory convergence. This permits explaining all the facts regarding adaptive modification and plastic readjustments of the visual cortex neuron RFs as well as their dynamics in time microintervals.

It seems, the concepts we have suggested can also account well for such long-lasting plastic readjustments of cortical neuron properties as those which occur during conditioning. The general principle of adaptive modification of functions we propose to discuss here is as follows. The most effective mechanism responsible for their performance apparently resides, chiefly, in intracortical inhibition whose function, as also in the case of RF formation, may be to block out the excitatory connexions that are 'excessive' in a specific situation, from the total number of strongly redundant connexions making the brain a rich nervous circuitry. If so, the conditioned specialization of the higher nervous functions must be due to the activity of the tonic inhibitory mechanism to which the main reflex conditioned processes and events are conveyed. In support of this proposition are well-known and convincing data on ontogenetic maturation of the cortical neuron RFs which comes as a result of both the genetic program, and sensory training and learning, with obvious and considerable involvement of inhibitory mechanisms. It remains to hope that future neurophysiological experiments will provide evidence in direct support, or direct refutation, of the current alternative views on these essential issues of cerebral activity.

For the moment, the assumption of real behavioural adaptive value for the neurophysiological phenomena revealed in this study seems to be substantiated by psychophysiological controls. In this regard, the coincidence of the qualitative, and in some respects also quantitative characteristics of neurophysiological and behavioural reactions looks rather encouraging for deriving further successful correlations of this kind. A stand-alone question in this context is whether line orientation coding is feasible not only with the place code, as it follows from the classic detector concept, but also with the temporal pattern code, which agrees with our data on dynamic 'resetting' of the orientational tuning of visual cortex neurons in time microintervals. Indeed, while the manifestation of the process in human behavioural reactions is documented well, psychophysiologically, its coding value still remains an open question. Hopefully, future investigations will produce positive evidence for the code's realistic rather than candidate character. Though, of course, such proof is also required, in the time being, for the overwhelming majority of other candidate codes suggested by neurophysiologists.

A necessary concluding note is that the research on flexibility, plasticity and dynamic properties of the neuronal structures responsible for central information processing is more than merely a fashionable trend in neurophysiology. The analysis of these properties, relevant to the activity of neurons and their populations, brings one closer to understanding the operation of the brain and

its systems not in idealized, simplified and constrained situations, but in situations approximating reality, with broad variability of the environment, state of the organism, character of the problems it has to deal with under specific conditions, and priorities in concurrent operations. If seen in such a perspective, the future of the neurophysiology of brain information processes lies exactly with this kind of research.

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## Interaction of Inborn and Environmental Sensory Factors in Ontogenesis of Behaviour in Mammals and Birds

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### 5.1. GENERAL DESCRIPTION OF ALIMENTARY BEHAVIOUR IN NEWBORN MAMMALS

Alimentary behaviour is one of the few inborn patterns that are already highly organized by the time of birth. Dynamically variable motor and sensory components of the food acquisition function as well as unavoidable contacts with siblings and also with the mother make food acquisition a singularly fortunate model for research into inborn and environmental factors in the development of behaviour.

Ontogenic sources of the food acquisition function have their origin in the early stages of prenatal life. The first feeding reactions appear as fragments in a 10-week human foetus and a 30-day cat foetus. The human baby is born with a capacity to produce a 'vacuum' in the mouth once he has grasped the nipple, and then with the help of rhythmical sucking movements to obtain milk performing complex coordination in the work of chewing, swallowing and respiratory muscles. If given a sour- or bitter-tasting liquid instead of milk, the newborn, from the very first feeding, even though he may not have tasted milk before, spits out the teat and exhibits mimical and vocal reactions, indicating that he does react to the substitution and that gustatory food characteristics are genetically programmed in him (Fig. 5.1,4).

The following days witness a fairly clear picture of behavioural patterns reflecting the processes of learning. These include the appearance of sucking movements as the reaction to the time, posture or procedure of feeding. The sucking movements in feeding are becoming finely adjusted to the flow rate of milk from the maternal breast or bottle. Elements of active searching begin to be observed as scanning head movements. In sucking they are apparent in massaging the maternal breast with finger movements. Adaptive processes in the function of respiratory muscles during sucking

become complicated. Thus the baby is able, and the adult is not, to swallow during the eating without inhibiting respiratory movements.

The feeding reactions in newborn mammals (kittens) typically show still higher motor activity. The newborn kitten, even before

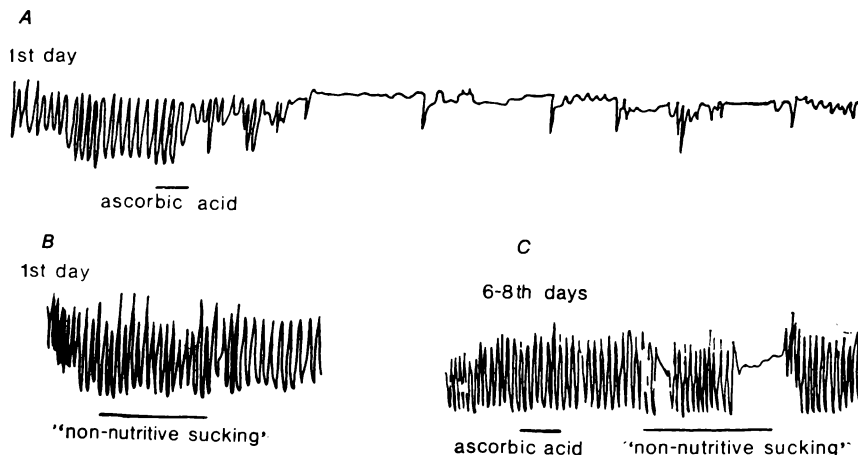


Fig. 5.1. Reorganization of the role of return information in sucking of the newborn infant.

A, C—sucking movements in milk sucking and after milk substitution by sour-tasting liquid (underlined); B, C—sucking of milk and of dummy (underlined). Age in days is shown on top of the curves

drying off, begins crawling about in search of his mother. He pokes his nose into her fur, making the characteristic head movements and rubbing in the area of her nipples. And all the while his four limbs either assist him with forward motion or strain in propping to support bodily balance.

The grasping of mother's teat is the main point in the succession of food-searching movements that signifies the shift to food intake. The latter occurs suddenly, has a reflex nature and is triggered by the sensory flow from the oral afferents. The onset of the sucking movements produces an abrupt change in the animal's behaviour: the kitten comes to a stand-still, shapes the tongue into a little groove along the nipple and starts to suck at the rhythm of one or two movements per second. Given high-level feeding motivation, it is typical to see the forelimbs moving to massage the mother's gland. This is not infrequently attended by a characteristic vocal pattern.

A question arises about the sensory mechanisms for the formation of food attributes by which the newborn finds and recognizes the food. What modalities signal the goal and what other modalities carry the information about the results, i.e. the location of food?



Anyone trying to imagine this complex sensory integration will be struck by the purely ontogenetic aspects of the problem. Indeed the attributes of the feeding source (mother) and the food itself (milk) are formed by many modalities: visual, olfactory, auditory, temperature, tactile, proprioceptive and gustatory. In adult animals these modalities bear a signal function in the realization of alimentary behaviour. In newborns, however, far from all of them are employed to achieve the same adaptational result, that is, to obtain food. While this is evident for some of the later-maturing distance receptors, such as vision and hearing, it poses another cardinal question: which of the sensory parameters are inborn signals of food and which become signals in the process of alimentary learning?

On the basis of experimental data, it can be concluded that mammalian newborns recognize the source of food (mother) by using tactile and temperature modalities. Warm fur is a most biologically significant signal so that any object possessing these properties is appraised as an attribute of the mother causing well defined searching (Uzhdaviny and Shepeleva, 1966). Some authors argue that olfactory signals take no part in the recognition of the mother in kittens in the first week (Freeman and Rosenblatt, 1978). The same can be said for the visual and auditory systems.

In mammals, the inborn parameters of food (milk) are programmed in the tactile and gustatory afferents which signal the presence of food in the mouth and its taste-related properties. The arrival or non-arrival of food in sucking are of no consequence at that time. The newborn sucks any object introduced into the mouth and develops equally vigorous sucking movements for any dynamics of the milk inflow, up to its complete cessation (in sucking the dummy). Conversely, the sucking movements will be inhibited if the nipple is greased with another substance or if a sour- or bitter-tasting liquid comes via the nipple (Fig. 5.1,A,B).

The principal role of the tactile and gustatory modalities agrees with the electrophysiological data obtained by Chernikov (1979) in our laboratory. By the evoked potentials and unit activity recording from relay nuclei in the kitten medulla and cortex, gustatory and tactile (to the touch) transmission from the tongue was shown to have matured by birth time, with subtle discriminatory tactile sensitivity maturing sometime later.

Inborn forms of alimentary behaviour are accomplished by conditioned forms from the moment of delivery. The process then is developing in two directions. First, the set of possible food signals broadens with greater maturity of the distance receptors (olfaction, vision, and hearing). Second, the olfactory mechanisms of the feeding reactions become more and more differentiated and economical. A relevant example is the appearance of a 'preference' for sucking of the 'own' nipple in the kitten (Rosenblatt, 1971), or

a strict conformity between the sucking movements and the dynamics of the milk inflow from the mother's teats in the human infant (Shuleikina, 1966).

These modifications are complemented by new sensory patterns, above all by the increase in the number of components comprising sensory signs of the goal and results of the action. Thus, the principal signal of the mother, which in mammals is warm fur, is supplemented by the mother's odour, and later by her visual image. Interestingly, animals first recognize the mother's smell and only then the smell of the milk (Uzhdaviny and Shepeleva, 1966).

Sensory mechanisms of learning have also been studied on the alimentary behaviour of the human infant. From the moment of birth the sucking function is influenced by two processes. Under natural nursing, the signals from the chemoreceptors gradually lose their significance, because the infant always receives a liquid with the same taste, milk, as the result of his sucking movements. But along with this, the information about the dynamics of milk inflow becomes increasingly important because, depending on the mother's individual features or on the beginning or end of nursing, the milk from the teats flows irregularly.

As a result, beginning from the 6th to 8th day, the baby stops reacting to a short-time substitution in the rubber nipple of a different-tasting liquid instead of milk but will stop his continuous sucking at once if the syringe with milk is replaced by a dummy. As distinct from a newborn's, his movements in sucking milk or the soother begin to show marked differences of rhythm and character (Fig. 5.1,C).

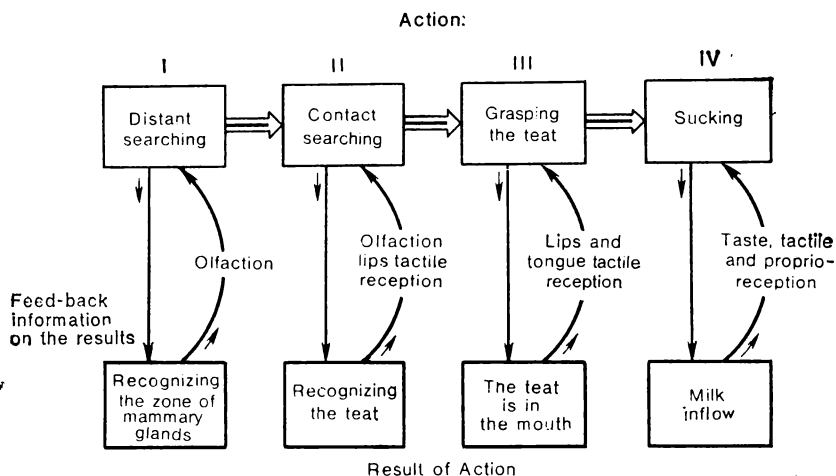
Nipple preference provides an excellent study model for the sensory mechanisms of learning in animals. It has been shown that a kitten learns to prefer his nipple by a sum of three sensory patterns: tactile, olfactory and kinesthetic. Should the tactile information be modified by shaving the fur around the nipple, the kitten will learn to find the nipple by its smell. If the nipple and the surrounding surface are deprived of smell the kitten takes one or two days to locate the nipple by tactile signals. If, in nursing on an artificial mother, both the tactile and olfactory attributes of the preferred nipple are altered arbitrarily, the kitten will all the same learn to find his way to it by orientation to kinesthetic signals (Rosenblatt, 1972).

Such results raise questions of major theoretical importance: how does behaviour change with sensory deprivation? To what extent are the consequences of the deprivation age- or modality-related?

The food search and intake of a kitten is divided into the following stages: distant search for the mother; contact search for the area of the nipples; grasping of the nipple, sucking and discontinuance

of food intake with satiety. As noted above, each of the stages is supported by its own pattern of afferentations (Fig. 5.2).

In order to study the role of a sensory flow from oral afferents, Shuleikina (1972) and Dyachkova (1976) performed anaesthesia of the perioral region and tongue by applying a 2 per cent cocaine



**Fig. 5.2.** Diagram of searching for food and food intake behaviour and the feed-back afferent flows that direct it. The kittens 1-30 days of age.

solution over the area of the lips and tongue. It was shown that under the local exclusion of the perioral area kittens lose the capacity for oriented distant search and begin looking for the nipple all over the body of the mother cat. In the majority of cases he fails to locate and grasp the nipple despite persistent searching. A finding of principal importance has been the observation of this phenomenon also in more adult animals homing in by visual signals. Under the local exclusion of the receptors of the tongue the kitten retained the ability to orient distantly, searched only in the teat area, and after some time found the teat and grasped it. In some instances, however, this made him lose the capacity to search for the preferred teat and in some experiments disturbed the rhythm and permanence of the sucking movements. Receiving no feed-back about the results of sucking, the kitten began to worry, gave up sucking and resumed the search.

Similar results followed the transection of the n. lingualis and chorda tympani. In kittens up to five days the transection led to the death in 50 per cent of cases. In more adult animals subject to treatment the behaviour recovered four to five days after surgery. But whereas the activation of food-searching behaviour was still observed

after anaesthesia of the tongue, the activity of food-getting behaviour was markedly reduced after transection of the n. lingualis and chorda tympani, while in the kittens few days-old it disappeared completely (Dyachkova, 1976).

The next series of experiments was carried out to study alimentary behaviour under olfactory deprivation of a kitten by intranasal application of a 5 per cent zinc sulphate solution. An isotonic

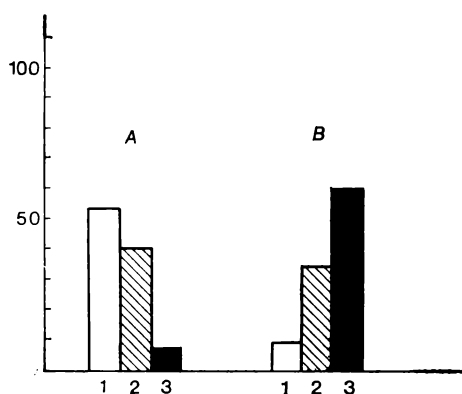


Fig. 5.3. Change of feeding behaviour in kittens exposed to olfactory deprivation at age 1-15 (A) and 15-30 (B) days.

1—not searching and not grasping the nipple; 2—searching but not grasping; 3—searching and grasping. The ordinate is number of animals in per cent.

solution or distilled water was administered intranasally to animals of the control group. Complete or partial olfactory anaesthesia resulted in 84 per cent of the kittens 24 hours following zinc sulphate irrigation, which on average lasted 72 hours.

In order to determine how this modifies alimentary behaviour one of the deprived kittens was weaned from the nipple and placed near the cat on her back. The kittens exposed to olfactory deprivation showed markedly different behaviour than the intact or control animals. The latter located the nipple areas and grasped the nipple within 60 to 90 seconds in 100 per cent of the cases. The kittens deprived immediately after birth and before the first feeding were unable to grasp the nipple and died unless artificially fed. With the deprivation sometime between the 1st and 15th days in a kitten already having some natural sucking experience (Fig. 5.3,A) 53 per cent of the animals still failed to reach the nipple area and therefore to grasp the nipple; 40 per cent of the kittens did find the nipple but could not grasp it; and merely in 7 per cent of the kittens was nipple searching and grasping undisturbed. Kittens deprived between 15 and 30 days (Fig. 5.3,B) were found in-

capable of reaching the nipple area and grasped the nipple in only 8 per cent of the cases; in 33 per cent of the cases the test animals effectively located the nipple area but could not grasp the nipple; in 59 per cent searching and grasping of the nipple were successful.

Thus, olfactory deprivation is most disruptive of alimentary behaviour in younger kittens (1 to 15 days) and less so in the adult ones (15 to 30 days).

Since from the very first day olfactory deprivation disturbed most the processes involved in the search for and grasping of the nipple it may be stated that, in contrast to the above data, olfactory afferentation constitutes a considerable element of the food-getting behaviour in the kitten.

A minor disturbance in the alimentary behaviour after olfactory deprivation in adult animals may take place because the visual system comes into play, whose role is to provide compensation if olfactory orientation is impossible. It should be noted that failure of olfactory deprivation did not disturb the proper processes of sucking and swallowing. Finally, the artificially-fed deprived kittens showed comparatively normal growth and development (Lushchekin, 1981).

## 5.2. SENSORY ORGANIZATION OF HOME ORIENTATION IN THE KITTEN

An increasing number of researchers have recently come to recognize the existence of another type of behaviour, the so-called home orientation, or 'home acquisition', in the early postnatal ontogenesis of mammals. Described with reference to the domestic cat, this type of behaviour was taken to refer to the kitten's ability, from the first day of life, not only to recognize his mother and find the nipple, but also to differentiate the attributes of his 'own' and 'another's' home site and, after being removed from the nest a few days later, to be able to locate the nest by sensory cues—thermotactile, olfactory, and visual.

Home orientation (HO) first emerges in 3- to 5-day kittens but the success in reaching the home area is extremely low (10 per cent at most). By the age of nine days the proportion of successful home area finding increases to 40 per cent (Fig. 5.4, 2). At that time the trajectory of the movements in the experimental field had a circular pattern. On the 15th to 18th day home area finding becomes most effective, accounting for 86 per cent on the 18th day. The animals in the experimental field show less anxiety and the trajectory of movements in the home area finding is rectilinear. By the 30th day the level of success in home area finding declines gradually to 50-55 per cent. In time, this coincides with the ini-

tial period of dominance by orienting and exploratory behaviour in the kittens and, as a consequence, they do not stay long in the nest and try to get out.

Guided by data suggesting that olfaction plays the key role in effective homing (Rosenblatt, 1976) we conducted a series of experiments with olfactory deprivation. In the olfactorily deprived animals up to the age of nine days home orientation did not show up at all and from age 9 to 15 days home area

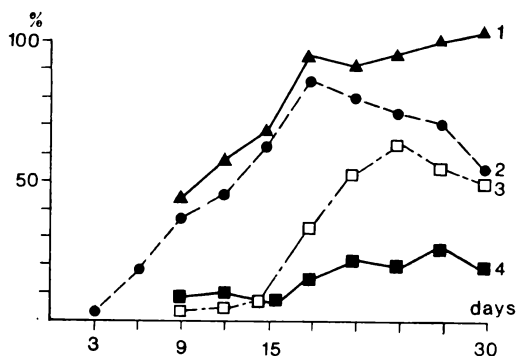


Fig. 5.4. Successful quest for home area as a function of age in intact and deprived kittens.

1—visually deprived kittens; 2—intact; 3—olfactorily deprived; 4—olfactorily and visually deprived. The abscissa is age of animals.

acquisition was successful only in some cases (Fig. 5.4,3). From the age of 18 days home orientation grew in effectiveness reaching a 60 per cent maximum on the 24th day and then gradually decreasing until settled at 50 per cent by the 30th day, as was the case in the control group.

It thus may be suggested that the role of olfaction is crucial for homing during the first 1 to 18 days, until the visual function becomes established so that later vision can compensate for the lack of information from the olfactory receptors. To check the suggestion, a series of experiments were performed with additional visual deprivation achieved by glueing the kittens' eyelids at the age of 4 to 30 days with БФ-6 Butwar-phenolic adhesive and coating a layer of rubber paste 88-N over it. The experiments revealed that simultaneous olfactory and visual deprivation of both 9-15 and 15-30-day kittens caused home orientation to almost disappear in all of them (Fig. 5.4,4). Consequently, during home orientation the olfactory and, from the age of 18 days, visual receptions move to the fore as the leading afferentation. But in the period under investigation the kittens also possess a sufficiently developed

auditory reception, in addition to the olfactory and visual reception (Gottlieb, 1971a; Olmstead and Villablanca, 1978). Nevertheless, there are no published data on the role of this particular modality in the organization of homing behaviour.

In another series of experiments we attempted to answer the question whether, at the period of 1 to 30 days of age, kittens possess orientation to the mother's vocalization. What is the dynamics of the acoustic orientation and in what way is sound-directed behaviour interrelated to the orientation by the olfactory and visual features of the nest?

Sound stimulation was provided by a speaker encased into a polaron capsule with a slot collimator installed in the home area. The source of acoustic stimulation came from previously tape-recorded sounds of the mother cat as she communicated with her kittens. To analyse the parameters of the signals they were later processed on a sonograph.

Two types of sounds were identified as emitted most often by the mother cat. Signals of the 1st type, in their basic modification (Fig. 5.5,A,B), are, as a rule, low-frequency, below 1.5 kHz, fricative sounds of low intensity; they are made by the mother cat when nursing the kittens (purring).

Signals of the 2nd type represent short, tonal calls of moderate intensity, with three or more harmonics whose respective energy maximums occur at 1, 2.5, 3.5 kHz (Fig. 5.5,B). The signals are produced by the mother cat when her kitten is taken away or hidden and are in effect her calling cries.

The experiments showed that, beginning with the 5-7th day, the kittens are able to find the nest by the orientation to the mother calls alone. However, with totally unimpaired olfaction and vision, from the age of 8 to 10 days, the percentage of correct responses to switched-on species-specific sounds was also higher than for the home orientation without the use of the sounds (Fig. 5.4,2, Fig. 5.6,7). The reaction to the species-specific sounds appears simultaneously with the reaction of nest-searching by olfactory cues (from the 6th day). Scanning head movements in kittens of an early age were a characteristic feature for both orientations (by sound and by smell). As was mentioned above, olfactorily deprived kittens lost the ability for home orientation and there were no scanning head movements. If, however, the olfactorily deprived kitten is presented with maternal calls his home orientation resumes (Fig. 5.6,2), as well as the scanning head movements. This allows the conclusion that maternal vocalization is also one of the stimuli that ensure the kitten's spatial orientation and participate in the nest-finding reaction.

The subsequent experimental series inquired into the home orientation ability of the visually deprived kittens presented with the cat's

acoustic signals. The findings have indicated more effective home area location by the kittens 9-15 and 15-30 days of age on presentation of both the 'food-related sounds' and calls (Fig. 5.6, 3). This

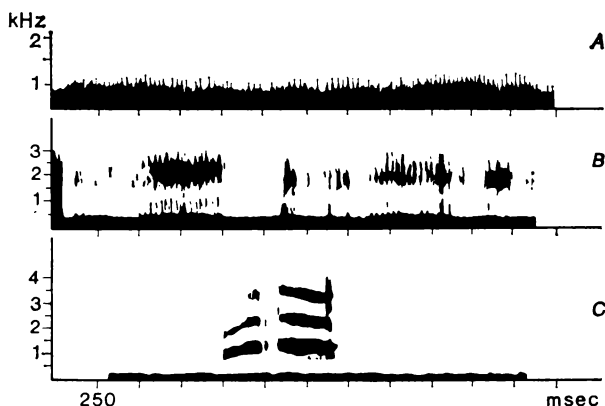


Fig. 5.5. Sonogram of species-specific signals of the mother cat in communication with her kittens.

**A** and **B**—purring; **C**—calling cry. The abscissa is time in msec, the ordinate is frequency in kHz.

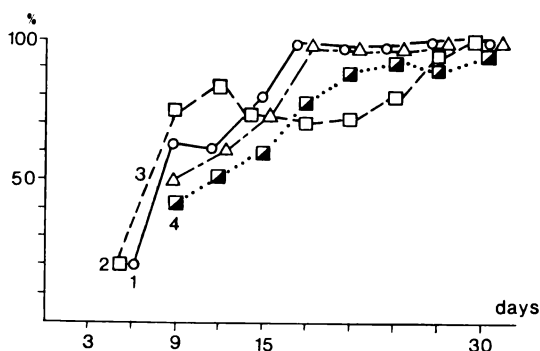


Fig. 5.6. Successful quest for home area as a function of age in kittens guided by species-specific calls.

1—home orientation in acoustically stimulated intact kittens; 2—same, for olfactory deprivation; 3—same, for visual deprivation; 4—same, for olfactory and visual deprivation. The abscissa is age of the animals.

proceeded with an even more pronounced homing reaction to the sounds than that of the intact animals: when presented with the calling sounds the 20-30-day-old kittens promptly came up to the speaker and poked their noses at it letting out intensive vocal responses. When the speaker was moved the kittens followed it even



beyond the home area, and a similar reaction was observed in the visually deprived two-month-old kittens in whom home orientation would normally no longer be manifest.

The above data favour the notion that olfactory and, at later stages, visual signals, have priority in the home orientation of a kitten. Lacking these, the home orientation may still successfully proceed by sound. The cat's species-specific vocalization reinforces the acoustically, visually and/or olfactorily guided homing.

### 5.3. GENERAL DESCRIPTION OF ALIMENTARY AND DEFENCE BEHAVIOUR IN EARLY ONTOGENESIS OF BIRDS

The relationship between the development and the subsequent increasing organizational complexity of natural behaviour was followed up further in the studies of four species of tree-hollow nesting birds: pied flycatcher (*Ficedula hypoleuca*), great tit (*Parus major*), redstart (*Phoenicurus phoenicurus*) and cuckoo (*Cuculus canorus*). The studies emphasized the development of a sensory basis for alimentary and defence behaviour—the two leading behavioural types of early ontogenesis. The nestlings of hollow-nesting birds proved a good choice for the object of the investigation for two reasons: first, their entire nest developmental period unfolds in a relatively stereotyped environment and, second, their living space is rigorously limited by the walls of the hollow or the nest box. Methodological conditions for the conduct of the experiments were published previously (Khayutin and Dmitrieva, 1976, 1981).

Investigation of the nestlings' behaviour in their natural habitat has established that during the very early period after hatching, their one and only developed reaction is a feeding reaction produced in response to sound stimulation. Up to the age of 5-6 days, the period of eye opening, alimentary behaviour is induced by exposure to a series of stimuli: tapping of the feet on the hole entrance (the sound, but not the shaking of the nest!) as the bird with food flies into the nest box; rustle of the nest material as the bird hops on it from the edge of the hole entrance, and a specialized 'food' call generated by the bird. The latter stimulus, however, occurs only in 50 to 75 per cent of all incidents of feeding. The spectral make-up of the components in the acoustic complex of the feedings for the examined avian species is presented in Table 5.1 and Fig. 5.7. Recording and analysis of the food calls produced by a large number of flycatcher and redstart individuals (in 100 birds) has led to the identification of several variants of the sounds with a different rate of occurrence. Therefore the 'acoustic complex

of the feedings' is represented by a sequence of wide-band sounds of different origin. The last of the components in the sequence has at least three variants in flycatchers and redstarts. The correlation of the spectral characteristics of all components in the complex for each of the three species finds the latter to comprise a continuous series from 0.2 to 8.0 kHz.

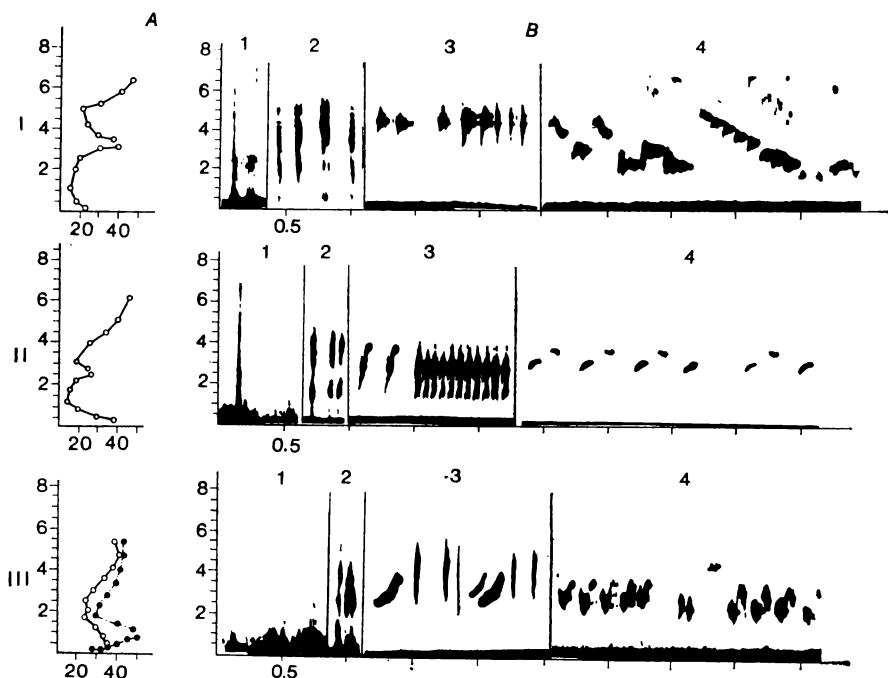


Fig. 5.7. Frequency-threshold characteristics of auditory sensitivity in 1-5-day nestlings of four species (A) and sonograms of behaviourally meaningful adult birds' signals (B).

A—the abscissa is sound intensity, dB (sound pressure over level  $P = 0.00002$  Pa); the ordinate is sound frequency, kHz; III—black circles identify the auditory sensitivity of cuckoo nestlings and light circles the auditory sensitivity of redstart nestlings; B—1—thump of feet on the hole entrance and rustle of nest material; 2—food calls; 3—alarm call; 4—specific song; I—pied flycatcher, II—great tit, III—redstart.

A laboratory assessment of the modality and parameters of the effective stimuli to give rise to the feeding reaction in 1-5-day nestlings has shown the reaction in flycatchers, redstarts and great tit, which can be evoked in response to sound signals alone (for cuckoo nestlings the shaking of the nest can also yield a full-scale feeding reaction). Besides the components of the sound complex of the feedings (reproduced from a magnetic tape) the reaction in the nestlings with a maximum high-level motivation is initiated by

**Table 5.1.** Characteristics of the Signals (in kHz) of Three Avian Species Meaningful for Their Nestlings' Behaviour and Characteristics of Auditory Sensitivity in 1-5-day Nestlings of Four Species

Species	Acoustic complex of feedings			Alarm call	Species-specific song	Auditory sensitivity of nestlings
	thumping	rustle	'feeding' call			
Pied flycatcher	0.2-1.2 1.5-3.5	0.2-1.0 2.0-2.5	1.5-2.8 3.0-5.5	4.5-5.5	2.5-4.5 5.5-6.5	0.1-3.0 3.5-6.0
Great tit	0.2-7.0	0.4-0.9 1.4-3.0	1.5-6.0	2.0-4.5	2.5-3.8	0.2-2.8 3.2-6.0
Redstart	0.2-2.0 2.8-3.2	0.2-1.5	0.8-1.5 2.0-4.5	2.5-5.0	2.0-3.5	0.2-0.8* 1.2-5.1* 0.1-0.5 0.8-5.1

\* The auditory sensitivity of the cuckoo nestlings reared in redstart nests.

a large set of other sounds such as whistles, speech, and various 'mechanical' sounds. Only acoustic stimuli, e.g. neither tactile including blowing-on a flow of air), nor vibrational or visual, produce the feeding reaction in the nestlings of all three avian species at that age.

Experimental investigation of auditory sensitivity in 1-5-day nestlings was conducted in the laboratory. Nestlings had electrodes implanted in their neck muscles and electromyographic expressions of their feeding reaction were recorded. Pulses were monotonal with a carried frequency from 0.1 to 8.0 kHz. Their duration of 50 to 75 msec was therefore consistent with the length of the typical species-specific calls. The criterion of the auditory sensitivity in each frequency range was 80 per cent reproduction of feeding reactions to the tone of minimum intensity by the nestlings with the highest feeding motivation level. The auditory sensitivity range for the nestlings of the target species was tabulated in Table 5.1 above and shown in Fig. 5.7.

From the 5-6th day the nestlings open their eyes (in the great tit nestlings the process was complete by the 10th day of life), thus effecting a change in the make-up of the stimuli effective in eliciting the feeding reaction. The species-specific feeding calls are never employed in practice anymore because the reaction arises in response to a simultaneously presented complex of the foot thump on the hole entrance and a short change of luminosity which occurs, now as before, in consequence of the entrance closure by the body of the bird as it flies in with food. Nevertheless an experimentally effected change of luminosity, in the absence of any sound whatever, evokes full-scale feeding reactions in the nestlings.

In determining the parameters of the visual stimuli that effectively cause the nestlings' feeding reactions in their natural habitat the following findings were obtained. The maximum magnitude of the background luminosity recorded on the eye level of the nestlings in the state of rest reached 180 lx. At the moment of the entrance closure by the body of the alighting bird it drops to 0.25 lx. Thus the luminosity decrease at the entrance equalled 3 log.units. The minimum luminosity decrease recorded in one of the tree-hollow nests was as low as 0.3-0.4 log.units. As for their duration, the luminosity drops were estimated as one half of the period elapsed from the moment the feet thumped on the hole entrance up to when the nest material began to rustle as the bird hopped onto it, which amounted to 125 and 150 msec. Thus the luminosity drop of 3.0 to 0.3 log.units and 125- to 150-msec-long provides the major single stimulus for 5-9-day nestlings.

Simultaneously with the period of opening the eyes and changing the modality of the triggering afferentation the nestlings' behavioural repertory becomes increasingly more complex. From that time onwards they begin to show a passive defence response to the alarm call issued by the adult birds outside the nest. The characteristics of the spectral make-up of the alarm call for the three avian species are summarized in Table 5.1 and Fig. 5.7. An outward form of the passive defence response of the nestlings of the three species being discussed is that they suspend the background vocalization and lie low during the exposure to the alarm call. In simultaneous exposure to the feed and alarm calls, two signals of different biological quality, the resultant behavioural effect is reduced to either reaction, depending on the level of the nestlings' feeding motivation and the duration of the alarm call exposure. In the nestlings with the compensated level of feeding motivation the feeding reaction is suppressed completely. An increasing level of the motivation produces the feeding reaction deprived of the vocalization component and with any further buildup of the motivation a full-scale feeding reaction ensues (Fig. 5.8).

With the emergence of two behavioural patterns—alimentary and defence—the specific song, until that time a totally ineffective factor in the nestlings' behaviour, begins to play a role in their interaction.

From then onwards and to the end of nest life the specific song acts to modulate the sensory, motor and emotional activity of the nestlings and thereby promotes the conversion of the behavioural integrations into one another. Besides, it constitutes a 'safety factor' due to its action that is antagonistic to the alarm call (Khayutin et al., 1978). Finally, the specific song performs an extra function for the great tit whose nestlings never leave the nest unless the specific song is in the background. The spectral characteristics

of this signal in birds of the target species are cited in Table 5.1 and Fig. 5.7.

From the 8-9th to the 13th day of life the nestlings' feeding reaction arises, as it did in the preceding period, in response to a change in luminosity, but is steered and sustained by the bird's moving silhouette. The beginning of that period sees certain changes altering the outward form of the reaction. Though the nestlings still

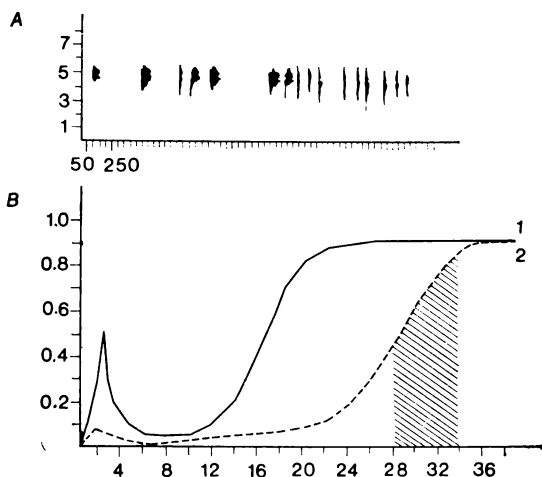


Fig. 5.8. Sonogram of species-specific alarm calls in pied flycatcher (A) and probability of feeding reactions in the nestlings experiencing adequate (visual) stimulation (B) presented singly (1) or against the background of alarm call (2).

A—the abscissa is time in msec; the ordinate is sound frequency, kHz; B—the abscissa is time in min, with the moment of feeding taken as 0, the ordinate is probability of the reaction. Shaded area identifies the period when food calls presented against the background of the alarm call initiate a reaction without vocalization.

lift their heads with wide-open bills, they do so not straight upwards as before, but orient them in the direction of the adult bird's head, vigorously attacking her beak and snatching out food. As a result their reaction gradually transforms from passive-feeding into the food-acquisition reaction proper. The new reaction form when analysed was seen to have two stimuli associated with its organization: triggering—the change of luminosity, and steering—the moving bird's silhouette. Either stimulus has an independent value of its own. The isolated change of luminosity induces an extremely reduced reaction, whereas the motion of a coniform object, imitative of the bird's silhouette, causes the nestlings to turn their heads and start to make pursuing eye movements without the posture, bill-opening and vocalization appropriate to the feeding reaction.

On the 13th to the 18th days, the final stage of nest life, the feeding reaction is produced and steered by the moving bird silhouette. The diffuse luminosity change ceases to be an effective

stimulus for the reaction. The passive defence reaction is still initiated by the alarm call as before.

To clarify the question as to what extent the maturation sequence of the sensory mechanisms underlying alimentary and defence behaviour in the nestlings is determined by genetic vs. environmental factors, a series of experiments was carried out on the flycatcher nestlings raised in a sensorily enriched environment. For that purpose, several families were formed consisting of different-aged nestlings (in one and the same nest). The age difference between the younger and older nestlings was a maximum of 4 days. In the course of this research it was found that in these conditions the nestlings in the younger age groups open the eyes much earlier, in fact as early as the end of their third day of life—the time when the passive defence reaction was also emerging. The shift from the feeding to the food-acquisition reaction and the departure

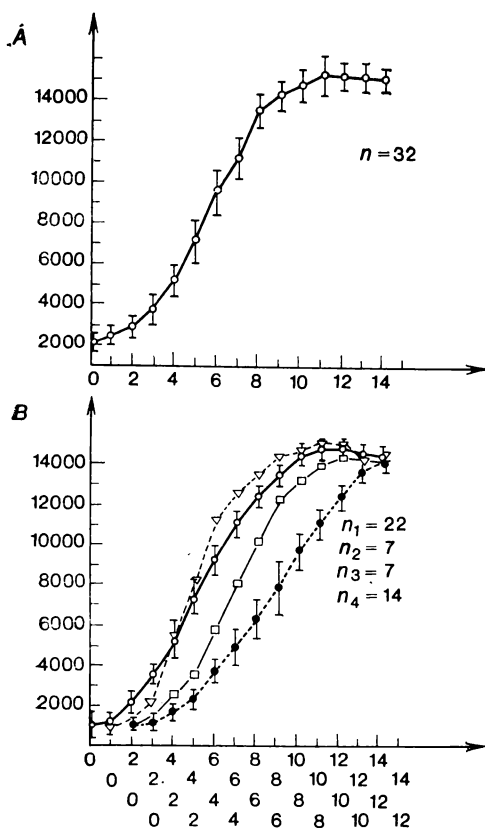


Fig. 5.9. Dynamics of body mass in nestlings through their nest life.

A—in families with natural synchronous hatching (all nestlings hatched within one day); B—in families artificially formed of different-age nestlings; the abscissa is nest life in days; the ordinate is nestling body mass in mg;  $n$ —the number of nestlings in every age group.

from the nest occur synchronously in the nestlings of the two age groups unless the age difference between them exceeds 3.5-4 days (Fig. 5.9).

Analysis of the experimental results indicates that in order to achieve full-scale physical maturation within a shortened time-

frame the nestlings of the younger age groups require a prolonged period of contact with the nestlings of the older age groups. Apparently, it is this contact that sets up the necessary prerequisites for the selectively accelerated (heterochronous—after Anokhin, 1949) development of the principal sensory and motor capabilities in the nestlings of the younger age groups. One may include among the factors accelerating the development of the nestlings their increased motor activity, a supplementary set of tactile and temperature influences brought about by the motion of the older nestlings, and the vocalization accompanying the feeding activity of the older nestlings from the first few days of life of the younger ones. The aggregation of these factors, which provides for the actuation ahead of time of the sensory and motor components of the nestlings' functional systems during their nest life, is considered as a physically and socially enriched environment. Thus, the findings gained from this experimental series suggest that the maturation rate of the sensory and motor mechanisms of the principal forms of behaviour in the nestlings may on a significant scale be contributed to the modified environmental factors involved. In all likelihood, the maturation sequence of the sensory mechanisms is predetermined by genetic factors, whereas the maturation rates of the same mechanisms follow the dictates of the physical and social environmental conditions.

Comparison of the factors contributing to the sensory organization of alimentary and defence behaviour in the nestlings of the tree hollow-nesting species, including the cuckoo nestlings reared by redstarts, throughout their entire nest life reveals some common features of basic importance to them. To begin with, the only form of behaviour fully shaped out in the nestlings at the initial period of life is the alimentary behaviour steered by acoustic signals. In all cases the alimentary behaviour is evoked by a set of wide-band sounds of different origin that are patterned together into a simple mechanical sequence. Experiments have revealed that under usual conditions (with the normal, 50-60 dB level of the acoustic background in the biotope) the behaviour can be realized by the action of any isolated component from among the set. The only factor responsible for the selectivity of the signals is the current level of feeding motivation in the nestlings. Generally one may assume that the set's initial components are more effective in case of a heightened level of the motivation and the final components when the motivation level is lowered. Therefore the complete make-up of the sound sets associated with the feedings, by virtue of being redundant, ensures a high reliability in the performance of alimentary behaviour. Moreover, the last component of the set, the food-related sound, which originates naturally, as a rule, when alimentary behaviour is already unfolding in the background under

the effects of the previous stimuli, only enhance it, due to its being supplementary and taking on therefore the role of a 'safety factor'. In equal measure, the high reliability applies to the frequency spectrum of the 'acoustic set of the feedings'. The reproduction of feeding behaviour by the nestlings in an experimental situation of exposure to the monotonal pulses that fall within the major portion of the spectrum of the food-related signals, attests additionally to the redundancy of the frequency set in all of the set's components without exception.

On the other hand, efficiency in reproducing the behaviour induced by atypical 'food' calls in the flycatcher and redstart nestlings is suggestive of two things. First, there may or may not be an all-round coincidence between the frequency spectrum of the behaviourally meaningful species-specific calls coming from adult individuals and the birds' perceivable range of frequencies. Second, in a broader sense, the stimulus in natural behaviour is only a gating factor for its performance, the goal (the receipt of food in the case in point) being the sole determinant in the organization of behaviour. Presumably, coincidence between one or several maximums out of the entire spectrum is enough to provoke goal-directed alimentary behaviour in its entirety.

There seems to be a measure of conflict between the supposition just made and the concepts, now gaining acceptance in the literature, that the range of frequencies perceivable by the nestlings just after hatching must match completely all spectral parameters of the species-specific calls of adult birds effective with regard to their corresponding behaviour (Milyagin, 1956; Konishi, 1970; Gottlieb, 1971b; Tikhonov, 1981; Golubeva, 1978). A more formal objection to the same concepts comes from one finding our work has demonstrated for the nestlings of all four species, namely, the sensitivity to low-frequency sounds. The sounds, which constitute the first two components of the set, are not species-specific in the strict sense and neither are they represented on the spectrum of the species-specific 'feeding' vocalization in the adult birds. It is contended that 0.2-1.0 kHz, the nestlings' range of auditory sensitivity, is in active use in the species' biology fully in agreement with the ecological distinctions of their habitat, mediating (by means of the genetic programme of embryonal development) alimentary behaviour to the obligatory set of sounds attendant on every arrival of the adult birds with food.

One could perhaps allow that the increased sensitivity the nestlings of all four investigated species show towards the range of the set's species-uncharacteristic components might result from learning in the period of late embryonal development. Evidence for such sensitivity is plentiful from the studies devoted to the ontogenesis of early behaviour in birds with different ecology. They suggest



that the late embryonal and early postembryonal sensory experience, chiefly acoustic, exerts a fundamental influence upon the organization of the subsequent, acoustically directed behaviour and, accordingly, upon the preference for sounds of definite structure and parameters (Gottlieb, 1971, 1979; Konishi, 1973; Vince, 1973; Impekoven, 1976).

So, the feeding behaviour of the nestlings just after hatching is provoked by a 'mechanical' sequence of relatively wide-band sounds ('frequency column', to use the figurative expression of Vince, 1973). By contrast, the passive defence reaction, seen to appear in the nestlings of all four species early in the latter half of their nest life along with the changing or expanding modality of the triggering afferentation of alimentary behaviour, arises in response to rhythmically organized signals. Furthermore, a unit pulse in the alarm call of the great tit is somewhat similar to the species-specific food calls. Unlike it, the vocalizations of the pied flycatcher and redstart show a marked difference between the feeding and defence calls. Finally, in cuckoo nestlings the alarm calls of all three avian species produce a passive defence reaction.

Lastly, the third type of species-specific calls, the specific song, an equally essential control of nestling behaviour, begins to play a specific role in the final stages of nest life. Though the particular importance of the specific song for organization of behaviour in the nestlings of the examined species varies, on the whole, between these species, the signal is polyfunctional in all instances, as compared with monofunctional calls—feeding and defence. As regards the signal's structural and rhythmical organization, it continues to increase in complexity while the frequency spectrum of its constituent single pulses narrows down further—the development most in evidence in the great tit.

In conclusion, there is a general trend towards an increasingly complex organization of acoustically steered behaviour in the nestlings' development. This runs parallel to growing sophistication of the pattern of its controlling signals and the latter's narrowing-down spectrum.

A similar tendency involves an increasingly complex organization of visually directed behaviour together with a more sophisticated pattern of its controlling signals. This, too, is an obligatory factor of ontogenesis in the four avian species examined. In the final stages of nest life there exist no other controls of alimentary (food-acquisition) behaviour in the nestlings of the four species but a structured visual environment. Incorporation of the organized visual environment into ontogenesis of goal-directed behaviour makes sense if there is appropriate visual experience gained by each species during critical developmental periods strictly fixed and delineated for it. Due to the effects of exogenous factors, the periods

may be shifted forwards or backwards: they are earlier organized (accelerated) where a specific, sensorily and socially enriched environment is set up; their organization is retarded when sensory and social deprivation is the case (see above). Up to now the formation from simple visual receptive fields of complex-organized ones adequate to the information content of the specific environment, and the influence of early visual experience upon the process has been proved for amphibians (Pomeranz, 1972; Dmitrieva, 1976) and a great many mammalian species (Buisseret and Imbert, 1976; Grobstein et al., 1975; Wiesel and Hubel, 1974). But probably birds also, including their hollow-nesting species, are no exception to the common rule.

Therefore, the growing organizational complexity of both acoustically and visually directed behaviour in early postembryonal ontogenesis applies in equal measure to the nestlings of the species discussed. As this goes on, the organization of sensory mechanisms and their mediated forms of behaviour enhances in scope and extent, making increasing organizational complexity of a specific environment ever more imperative.

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# 6

## Spatial Synchronization

### and Conditioned Reflex Formation

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The mechanism and localization of the process whereby temporary connexion takes form is a topical problem central to a series of studies in brain physiology. Despite recent spectacular successes in this area, aided by classical conditioning (Asratyan, 1970; Anokhin, 1968; Beritov, 1961; Belenkov, 1980) and electrophysiological methods (Livanov, 1972; Rusinov, 1969) much remains vague as yet, so a good deal more research will be required.

A more particular instance of a currently relevant issue in the neurophysiology of higher nervous activity central to related research is concerned with the interaction of the various brain cortical structures and subcortical areas in the process of the formation and realization of the conditioned reflex.

That the process of conditioned reflex elaboration and realization takes place with the interaction of different cerebral structures is evidently beyond question.

Proceeding from this, we based our investigations on the study of interrelations between bioelectrical processes of several cortical and subcortical structures. This research trend originated in the 1940's. At that time, visual EEG analysis demonstrated that in rabbits an elaboration of a conditioned defensive reflex to a rhythmical light stimulus (2.5-6 Hz) reinforced with electrical shocks applied to the paw skin at the same rhythm was accompanied by the acquisition of the same rhythm in the EEG of the appropriate neocortical areas (including visual and parietal), which was nowhere as pronounced as in its sensomotor region. The rhythm would appear, once the rabbit found himself in the experimental environment. The phenomenon was shown to have regular dynamic development (Livanov and Polyakov, 1945; Dumenko, 1955 [a, b]). The authors identified a generalization phase in which the acquired rhythms became broadly generalized throughout the cortex, involving not only the sensomotor, but the visual and parietal areas as well. This conditioning period involved the period of presentation from 40 to 70 pairings. This was when a conditioned behavioural reaction first appeared, its emergence consistent with the isorhythmical pattern flow of the bioelectrical process in the cortical areas of the motor and visual analysers.

With further elaboration of the conditioned reflex, the acquired rhythms disappeared from the neocortical potentials. The authors termed it a period of concentration. Yet a more detailed investigation into spatial distribution of the acquired rhythms in this region made it clear that in the period of concentration the acquired rhythms did not disappear totally from the potentials of the neocortex, the sensomotor area included; rather they became spatially delimited by the representation area of the rabbit's hind paw to which the unconditioned stimulus had been applied (Livanov and Ryabinovskaya, 1947, 1948; Livanov et al., 1951).

The conclusion drawn from the research findings stated isorhythmicity of the bioelectrical processes, those in the brain cortex as well, to be an essential factor in producing the temporary connexion. Even at that time the authors suggested, that the cause underlying the conditioned defensive reaction to a rhythmical conditioned stimulus, was a system of rhythms reflecting periodical excitability changes of the cortical centres—the basis of their isolability (Ukhtomsky, 1934, 1936).

The conclusion was confirmed in subsequent investigations using rhythmically discordant conditioned and unconditioned stimuli to elicit a conditioned defensive reflex in rabbits (Livanov and Korolkova, 1949, 1951).

Under such circumstances conditioning, as a rule, developed with great difficulty, if at all; besides, the rabbits exhibited trophic disorders, a reflection of their general neurotic state, and higher frequency waves appeared in the EEG of the cortical area involved.

Precise computerized mathematical analysis of the correlations of bioelectrical processes between different brain regions made it possible to show (Livanov et al., 1967; Livanov, 1972; Korolkova, 1977) that similarity between the potentials of brain structures reflected the condition for a functional connexion to be carried out between them.

This was our conclusion derived from the results of automated controlled experiments, when potentials of the visual and sensomotor regions in the rabbit brain cortex during the experiment were fed into the computer on line which kept an on-going continuous estimation of cross-correlation coefficients ( $\rho$ ) of their potentials with a 1.5 sec time epoch of analysis, using an overlapping method with a lag of 10 msec. Whenever their values fit those specified by the program (i.e. exceeded 0.7) the computer switched on light stimulations of an identical supra-threshold intensity and recorded the presence or lack of an orienting reaction; the latter was ascertained from EMG changes in the flexors of the paw contralateral to the recorded brain region.

This experimental arrangement made it possible to define a relationship between the probability of orienting movements and the

value of synchronism for oscillations of the potentials between target regions in the brain cortex.

Indeed, the findings revealed the presence of a reliable linear relation between the number of motor reactions in response to a light flash and the extent of synchronism in the potential oscillations of the investigated cortical regions.

It was shown positively that the higher the level of spatial synchronism between the potentials, the easier this would make the passing transmission of excitation from the visual to motor analyser.

A spectral analysis of the EEG associated with the states being studied indicated (Livanov, 1972; Korolkova, 1977) that the high  $\rho$  values in the rabbits in the periods just before presentation of exteroceptive stimuli corresponded to well expressed, indeed not infrequently dominant, theta rhythms in the visual and sensomotor region potentials and a high level of coherence in this frequency band.

It was thus established that the high degree of synchronization between the potentials of the cortical regions and their high level of coherence in the theta range in the period just before presentation of exteroceptive stimuli provided a condition favourable for the achievement of a functional connexion between spatially unconnected brain structures that were parts of different analysers.

In the belief that the degree of similarity between bioelectrical processes presented a condition fostering the probable appearance of an interconnexion between various brain structures, we studied the spectral-correlation characteristics of the potentials of both specific and non-specific brain structures in a rabbit, developing a conditioned defence reflex to non-rhythmical light with an electrical shock skin reinforcer applied to the paw.

Biopotentials were studied for the following brain structures: sensomotor (Sm), visual (Vis) and auditory (Au) neocortex regions; area CA<sub>3</sub> of dorsal hippocampus (DH), nucleus anteroven-tralis thalami (AV), midbrain reticular formation (RF) (tegmentum), nucleus basalis amygdalae (Am), nucleus medialis septi (Sp), and lateral geniculate body (LGB).

The study centered on the EEG spectra of the brain structures and the paired cross-correlation coefficients and coherence functions in the frequency range of 1.0 to 12.0 Hz.

The experimenters recorded in different rabbits 3, 4 and 5 bioelectrical processes in varying combinations but with the necessary participation, in each of them, of the EEG of sensomotor region as an element of the efferent part of the reflex.

The common characteristic of all background spectrograms prior to conditioning was the presence of delta- and theta-range frequencies. In these ranges the power spectra could be more or less vari-

able in form. Of the nine brain structures, the delta range was most prominent in the EEG spectrograms of RF, Am and Sp.

The spectrograms of 4-second EEG epochs for each rabbit on analysis revealed that in all the possible recordable combinations of the EEG of the various brain structures, namely: 1. Sm-Vis-Au; 2. Sm-DH-RF-AV; 3. Sm-DH-Am-Sp and 4. Sm-Vis-DH-RF-LGB the maximums of theta rhythm (if present in the spectrogram) were usually located (from 60 to 100 per cent) at different frequencies. In magnitude, frequency disagreement in the theta range could reach a maximum value of 4.0 Hz. In the background Sp potentials no theta rhythm was distinguishable, as a rule.

The degree of correlation between the bioelectrical processes as determined from the cross-correlation coefficients ( $\rho$ ) was dissimilar between different structures. The highest level (0.7 to 0.9) was observed most often between the AV potentials on the one hand and the Sm and DH potentials on the other. In the majority of cases, the  $\rho$  values proved to be the lowest ones, whether positive or negative (from  $\pm 0.1$  to  $\pm 0.2$ ), between the RF potentials and those of the other brain structures studied—Sm, DH, AV, and Sm, Vis, DH, and LGB.

Values of the coherence functions, reflecting the interconnexion of the bioelectrical processes at each of the frequencies to be defined, were unequal between the potentials of different brain structures. They varied from one experiment to another, and the correlations of the values of the coherence functions between different brain structures were the only ones to remain stable. They were the lowest (0.2 to 0.5) between the potentials of RF and Sm, Vis, DH, AV, and LGB, and the highest between the electrical processes of AV and DH, and Sm (0.6 to 0.8).

In the course of elaboration of a conditioned defence reflex, there was a slight (by 0.5 Hz) increase of theta-rhythm frequency in the potentials of the studied brain structures or expansion of the latter's amplitude in the spectrogram, compared to the other frequencies.

The most complete spectral analysis of biopotentials was made for the Sm-DH-RF-AV alternative. In that case it became evident that in the elaborated conditioned reflex the theta-range frequency, on averaged data for five rabbits, was equal and occurred at 5.5 Hz on the EEG spectrograms of Sm, DH and RF. A subsequent analysis of the relations between spectral functions (4-second EEG segments) for each rabbit disclosed a low percentage (from 0 to 25) of coincident theta-range frequencies between the EEG spectrograms of the brain structures under study at the stage of a developed conditioned reflex. The degree of correlation between the potentials ( $\rho$ ) persisted at its former high level between the AV and Sm, and DH potentials. The cross-correlation coefficients between

the DH and Sm potentials grew for those rabbits in whom they had been low in the background, but remained as high as before in the animals with initially high  $\rho$ . Between the RF potential and those of the studied Sm, DH and AV regions the cross-correlation level declined for the case of their initially high values and remained lowered in the animals with initially low  $\rho$  in the background.

Upon presentation of a positive conditioned stimulus, light, to a rabbit with a developed conditioned reflex, accompanied by a conditioned behavioural reaction (CS+), this would always accelerate the theta-rhythm frequency in the potentials of all brain structures involved (Sm, Vis, Au, RF, AV, LGB, Am and Sp) to its equal value. An analysis of the histograms of frequency distribution in the Sm, DH, RF, and AV EEG spectrograms identifies the frequency of 6.0 Hz (Fig. 6.1) to be the one most often present there. Moreover, the frequency was dominant in all of the studied areas, including RF, Am, and Sp.

Analysis of the 4-second EEG spectrogram segments indicated a significantly larger percentage of coincidences between theta-range frequencies in the potentials of all our studied brain structures during the effective time of the conditioned stimulus, as compared to the period that preceded CS delivery. It is interesting that the greatest percentage of the coincidences between theta-range frequencies (from 50 to 100) was found in those rabbits in whom the conditioned reflex was elicited most regularly and the percentage of its execution was higher in these rabbits than in other test animals (Efremova et al., 1979).

In the very first eight seconds after the pairings ceased, the frequency distribution in the EEG spectrograms of all the brain structures studied took on a form close to that in the period before CS presentation, i.e. the dominant theta-range frequency diminished to 5.0-5.5 Hz while the delta-range frequencies regained dominance in the RF, Am, and Sp potentials.

Therefore the data gained in the experiments suggest the alteration of bioelectrical activity in all of the studied brain formations during defence conditioning in rabbits. The changes comprise better expression and moderate acceleration (by 0.5 Hz) of the theta-range frequency.

In this way, on exposure to a positive conditioned stimulus with an accompanying behavioural conditioned response an electrographic reaction is observed in all studied brain formations both in the early period of conditioning and in the period of its stabilization as well.

A characteristic feature of the reaction is a narrow-band rhythm in the theta range found to have an identical frequency in the EEG spectrograms of all the studied brain structures. Relative to the period before the presentation of the conditioned stimulus, the for-



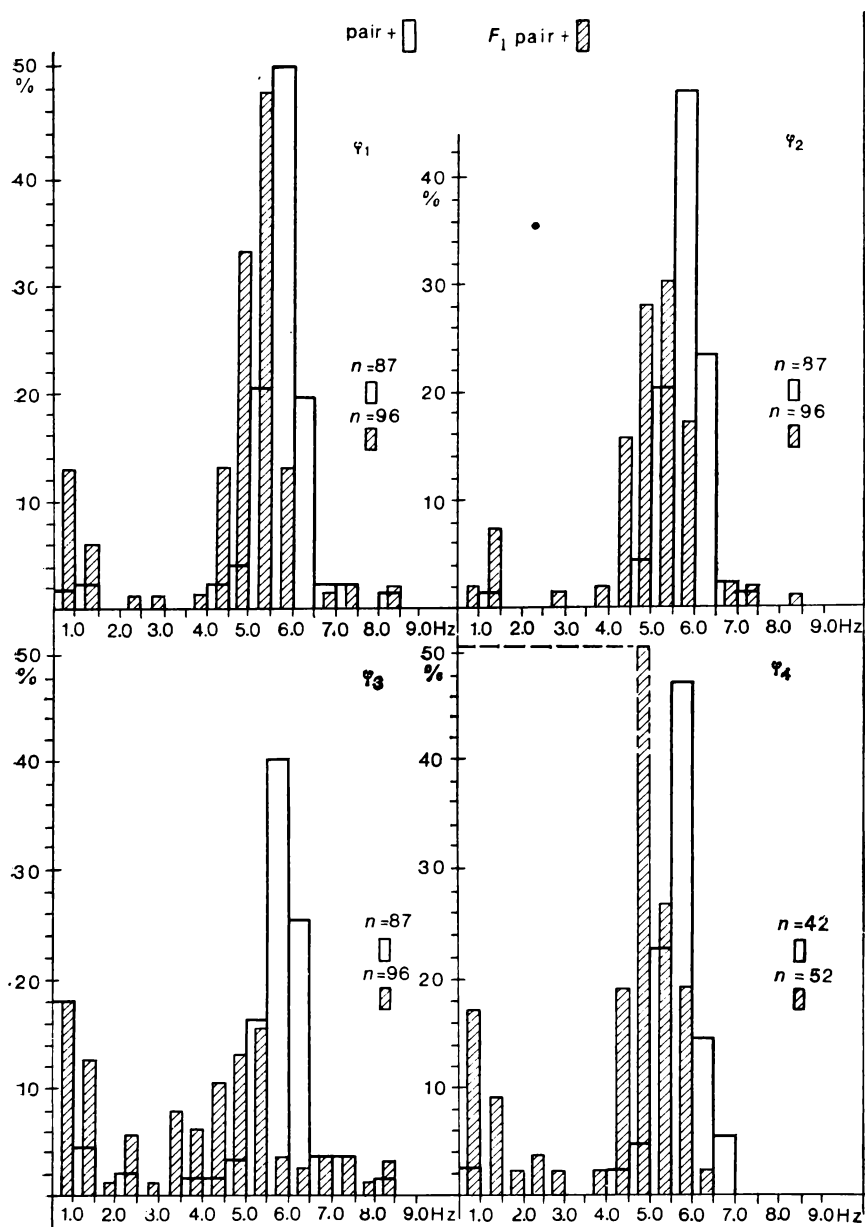


Fig. 6.1. Histograms of frequency distribution in EEG spectrograms of a rabbit in the period of exposure to positive conditioned stimulus (open square) and the period immediately before its presentation (hatched square). These are averaged data for five rabbits. The instances below correspond to the presence of behavioural conditioned response:

$G_1$  —  $n_1 = 87$ ;  $n_{11} = 96$ ;  $G_2$  —  $n_1 = 87$ ;  $n_{11} = 96$ ;

$G_3$  —  $n_1 = 87$ ;  $n_{11} = 96$ ;  $G_4$  —  $n_1 = 42$ ;  $n_{11} = 52$ .

The abscissa is frequencies in Hz. The ordinate is relative shares of respective frequencies.

$G_1$  — Sm;  $G_2$  — DH;  $G_3$  — RF;  $G_4$  — AV.

mer's frequency turned out to be by 0.5 to 2.0 Hz higher and equal to 6 Hz for the majority of cases.

The coherence level in the theta range between the potentials of all our studied brain structures in the effective period of the conditioned stimulus was enhanced and its maximum shifted gradually towards the higher theta-rhythm values, in line with the shift of the maximum for the autospectral functions.

The coherence level was lowest between the RF potentials and those of the other studied brain structures, but in that case the maximum value of coherence appeared in the theta range, and approximated zero in the remainder bands of the frequency spectrum.

The level of cross-correlation coefficients, indicative of the extent of the summary linear relationship between the processes in a broader range of frequencies (from 1.0 to 30.0 Hz) proved to be unequal for different brain structures. Its values fell to a minimum between the RF and other structures' potentials. This was paralleled by associated maximum phase shifts in the theta range ( $45^\circ$ ).

Thus, the changes in bioelectrical activity in the realization of a behavioural conditioned reaction amount to the establishment of isorhythmicity in the theta range of the studied brain structures with the greatest level of coherence concentrated in the same frequency.

The conclusion drawn from studies by Efremova and Trush (1971, 1973), Efremova et al. (1977), Efremova et al. (1979) are as follows. In conditioning a reflex to light reinforced with electrical pulses applied to the paw skin, cortical and subcortical formations become involved in the process both at its early and later stages. The structures involved belong to different brain systems, either specific or non-specific, and include: the sensomotor, visual, and auditory regions of the neocortex, areas CA<sub>3</sub> of the dorsal hippocampus; midbrain reticular formation; anteroventral nucleus of the thalamus; amygdala and septum. We believe it is the process in theta range that coordinates the activity of these formations into an integral functional system.

We are convinced of this by the fact that the theta rhythm is a global process widespread throughout numerous brain structures in a variety of behavioural situations in rabbits (Mamedov, 1969; Livanov, 1972; Kotlyar, 1977) and in other animals, particularly during spontaneous movements, emotional strain, in a state of attention, and realizing orienting and conditioned reflexes (Grastyan et al., 1959; Elazar and Adey, 1967[a]; Elazar and Adey, 1967[b]; Pickenhain and Klingberg, 1967; Lopes da Silva and Kamp, 1969; Vanderwolf, 1969; Preobrazhenskaya, 1974).

This conclusion is also confirmed by direct data on the importance of the time factor in transmission of excitation between distant brain regions; the neurons of two analysers, visual and

sensomotor, interact so that the greatest probability of response by one of them to another's excitation recurs at an interval of 200 msec, consistent with the quantization of the perception of impulse sending in the theta range (Livanov, 1975).

But apparently the functional integration of brain structures leads to the accomplishment of a conditioned behavioural act as long as there is a proper level of excitability of the brain structures comprising the conditioned-reflex functional system, sufficient to actuate it.

This view is also confirmed by the fact that the 6.0 Hz frequency is present in the potentials of all the studied brain structures in the majority of cases when a behavioural conditioned-reflex act is accomplished.

A frequency close to the previous one, 6.5 Hz, was identified also by other researchers (Elazar and Adey, 1967[a, b]) in the potentials of several limbic formations in cats when they perform correctly a conditioned-reflex task in conditions of free behaviour.

Experiments with driving rhythm via direct varying-frequency electrical stimulation of the medial septal nucleus in rabbits showed that stimulation with 7.0 and 9.0 Hz frequencies accelerated and those with frequencies below 5.0 Hz slowed down conditioning (Korinevskaya, 1978).

In this context, the results of a spectral and coherent analysis of the EEG of different cortical structures and subcortical brain formations made in certain types of internal inhibition are of interest (Efremova and Trush, 1974; Livanov and Efremova, 1980; Efremova et al., 1981). The analysis was performed on EEG auto-spectral functions of the sensomotor, visual and auditory neocortex areas, dorsal hippocampal area CA<sub>3</sub>, reticular midbrain formation, and anteroventral thalamic nucleus in various situations matching the state of internal inhibition in terms of behavioural expression.

In the early period of differentiation, when a behavioural reaction in response to DS exposure still persists, the latter induced changes in EEG frequency parameters of the studied brain structures which were similar to those observed on exposure to positive CS, accompanied by the behavioural reaction.

Not so in an elaborated differentiation when in response to the action of a differentiated stimulus (a sound) unaccompanied by a behavioural motor response (DC—) a regular decrease in the theta-rhythm frequency from its level at the period before DS presentation was observed and the modal value of the theta-rhythm frequency in the studied brain structures was reliably lower than on exposure to positive CS (Fig. 6.2). Depending on the brain structure, it assumed different values, from 4.5 to 5.5 Hz.

The average value of theta-frequency variation in the period of DS exposure was negative though its mode conformed to '0' (Table 6.2).

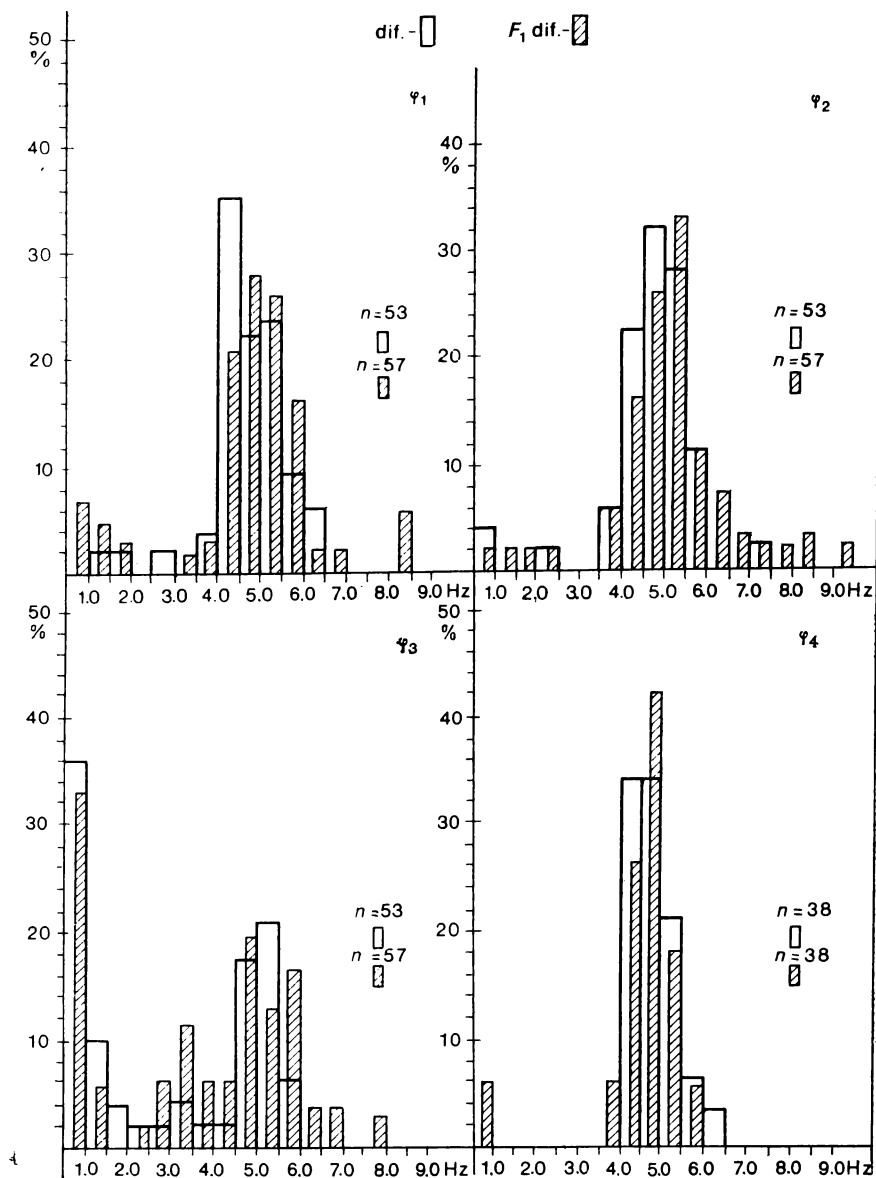


Fig. 6.2. Histograms of frequency distribution in EEG spectrograms of a rabbit in the period of exposure to differentiated stimulus (open square) and the period immediately preceding its presentation (hatched square). These are averaged data for five rabbits. The instances correspond to the absence of behavioural response reaction:  
 $G_1$  —  $n_1 = 53$ ;  $n_{11} = 57$ ;  $G_2$  —  $n_1 = 53$ ;  $n_{11} = 57$ ;  
 $G_3$  —  $n_1 = 53$ ;  $n_{11} = 57$ ;  $G_4$  —  $n_1 = 38$ ;  $n_{11} = 38$ .  
 Other designations are the same as in Fig. 6.1.

**Table 6.1.** Average Theta-Rhythm Frequency (f av.  $\theta$ ) in Different Behavioural Situations

No of situations	Type of situation	Brain region	Presence of conditioned-reflex reaction	$\theta$ rhythm, Hz	Error f av. Hz
1	CS	Sm	—	5.287	$\pm 0.059$
		DH		5.299	$\pm 0.053$
		RF		5.365	$\pm 0.109$
		AV		5.212	$\pm 0.054$
2	DS	Sm	—	5.103	$\pm 0.093$
		DH		5.070	$\pm 0.086$
		RF		5.208	$\pm 0.149$
		AV		4.868	$\pm 0.087$
3	CS	Sm	+	5.904	$\pm 0.062$
		DH		5.865	$\pm 0.045$
		RF		6.012	$\pm 0.065$
		AV		5.811	$\pm 0.075$
4	Background before CS—	Sm		5.153	$\pm 0.082$
		DH		4.966	$\pm 0.054$
		RF		5.391	$\pm 0.156$
		AV		4.951	$\pm 0.052$
5	Background before DS—	Sm		5.263	$\pm 0.129$
		DH		5.333	$\pm 0.120$
		RF		5.399	$\pm 0.140$
		AV		4.885	$\pm 0.072$
6	Background before CS+	Sm		5.148	$\pm 0.056$
		DH		5.157	$\pm 0.058$
		RF		5.328	$\pm 0.104$
		AV		4.882	$\pm 0.054$

Besides a decline in theta-rhythm frequency on DS exposure, there was a disagreement of the theta-range frequencies between the processes proceeding in the studied brain structures (Tables 6.3 and 6.4).

We subjected to separate analysis the cases with no conditioned movement in response to a positive conditioned stimulus (light) (CS—). We estimate these instances as a consequence of inhibition process in the CNS. The data of analysis showed that on exposure to the positive CS not accompanied by a conditioned behavioural reaction, the degree of theta-rhythm change in the po-

**Table 6.2.** Variation of  $\theta$ -Rhythm Frequency in Sm, DH, RF and AV Potentials Versus Previous Background in Different Behavioural Situations for 95 per cent Significance

No of situations	Brain region	Situation	Average value of $\theta$ -rhythm variation, Hz	Probability of random difference from background	Modal value of $\theta$ frequency variation, Hz
1	Sm	CS (+)	+0.63	0.0*	+1.0
	DH		+0.607	0.0*	+1.0
	RF		+0.792	0.0*	+1.0
	AV		+0.806	0.0*	+1.0
2	Sm	CS (-)	+0.211	0.005*	0.0
	DH		+0.333	0.0*	0.0
	RF		+0.042	0.73	0.0
	AV		+0.218	0.001*	0.0
3	Sm	DS (-)	-0.105	0.303	-0.25
	DH		-0.303	0.002*	-0.25
	RF		-0.047	0.664	0.0
	AV		-0.007	0.937	0.0
4	Sm	Extinction (-)	-0.238	0.02*	+0.25
	DH		+0.275	0.018*	+0.25
	RF		+0.300	0.015*	+0.25

\* Significant differences  
(+) or (-) Respectively, presence or absence of behavioural reaction in response to the use of the stimulus so marked.

**Table 6.3.** Coincidence of  $\theta$ -Range Frequencies between Sm, DH, RF and AV Potentials in Different Behavioural Situations

No of situations	Nature of EEG segment	Presence of behavioural reaction (paw flexion)	Coincidence of $\theta$ -range frequencies, %
1	CS	+	97.1
2	Background before CS (+)		56.4
3	CS	—	70.9
4	Background before CS (-)		54.2
5	DS		45.8

**Table 6.4.** Comparison of Degree of Coincidence of  $\theta$ -Range Frequencies between Sm, DH, RF, and AV Potentials in Different Behavioural Situations According to  $X^2$  Criterion for 95 per cent Level of Significance

No of situations compared	Situations compared	Probability of random difference
1	CS (+) and CS (-)	0.0*
2	CS (+) and DS (-)	0.0*
3	CS (+) and background before CS (-)	0.0*
4	CS (-) and DS (-)	0.0151*
5	CS (-) and background before CS (-)	0.0042*
6	Background before CS (+) and background before CS (-)	0.2339

\* Significant difference

tentials of the investigated cortical formations and subcortical brain structures occupied an intermediate position between what had been observed for CS+ and DS—; in other words, in some cases we encountered a slight increase of theta-rhythm frequency but not nearly as much as in the incident with a conditioned movement, while in some other cases the theta rhythm frequency became lowered.

Examination of the histogram of theta-rhythm change in response to CS in the absence of a conditioned behavioural response revealed its modal value to be zero, i.e. that in most cases the theta-rhythm frequency does not change in response to CS from the period before the stimulus was presented. However, the average value of the theta-rhythm change in response to CS— had moderately low positive values (Table 6.2). The extent of similarity between the processes in the theta range in the CS— situation occurred also in the intervening position between CS+ and DS— (Table 6.3).

In the extinction of a conditioned reflex the dynamics of theta-rhythm change in different cortical structures and subcortical formations involved followed the same regular pattern as in differentiation (Table 6.2).

Thus the analysis of the reviewed results demonstrates that the action of both positive and negative conditioned stimuli or, from the behavioural perspective, both the active state attended by a conditioned behavioural act and the internal inhibition state, manifested as the lack of conditioned behavioural response, give rise to a theta rhythm in the potentials of different cortical structures and subcortical formations of the rabbit brain, including the sensorimotor, visual and auditory neocortex regions, dorsal hippocampal

area CA<sub>3</sub>, midbrain reticular formation, anteroventral thalamic nucleus, lateral geniculate body, amygdala and septum.

There is a substantial difference, however, between the electrographic parameters reflecting the value of the theta-rhythm frequency and the correlation between the processes in the theta range in different brain regions appropriate to these two functional states.

First, the active state is accompanied by a high-level similarity in the theta-range processes between the cortical structures and subcortical brain formations and, conversely, a disagreement with these processes is observed in the inhibition states—on exposure to differentiation and extinction stimuli or a positive conditioned stimulus unaccompanied by conditioned behavioural reaction.

Second, the theta-rhythm frequency appears to be significantly higher in the former than in the latter case.

These findings give grounds to believe that various regions of the cerebral cortex as well as subcortical formations belonging either to the specific or non-specific brain systems are involved in conditioning both at the early and later stages of the process. We consider that the activity of these formations integrates into a common functional system by some processes, theta rhythm included.

The fact that theta rhythm constitutes a global process spreading far and wide through many brain structures in different behavioural situations, in particular during conditioned reflex formation and realization, confirms our assumption.

In support of the inference are also the data above, which attest to disturbance of isorhythmicity in the theta range between the processes in the cortical and subcortical brain formations in the states accompanied by inhibition processes (with the developed differentiation and extinction) (Efremova and Trush, 1974; Livanov and Efremova, 1980; Efremova et al., 1981).

Direct evidence supporting the proposition that theta rhythm is a process functionally integrating different brain structures for the realization of a particular function is the fact discovered in the analysis of interaction between pairs of neurons from the visual and motor analysers (Livanov, 1975).

As it turned out they interact in a way whereby maximum probability of response by the second neuron to the excitation of the first (in the sensomotor cortex) occurs at an interval of 200 msec, in line with the quantization of the perception of an impulse sending in the theta range.

But the functional integration of the brain structures would seem to bring the accomplishment of a conditioned behavioural act if there was an adequately high level of excitation of the brain structures constituting the conditioned-reflex functional system which is sufficient to actuate it. This is confirmed by the observa-



tion that in the majority of cases when a behavioural conditioned act is performed there was a high theta-rhythm frequency, i.e. 6 Hz, in the potentials of the studied brain structures (Efremova et al., 1979). A frequency of 6.5 Hz approximating the former was observed by other authors (Elazar and Adey, 1967) in the potentials of several limbic formations of cats as they perform correctly a conditioned-reflex task in free behaviour.

To be added to this is the finding that the spatial equality of theta rhythm oscillations in amplitude has a major role in the spread of excitation (Knipst et al., 1976; Balashova and Vasiliev, 1977).

An investigation of the thresholds of motor reactions to direct electrical stimulation of rabbit sensomotor cortex revealed that these thresholds are reduced with increasing synchronism of the cortical potentials involved (Korolkova, 1977).

Whenever a behavioural conditioned response to the same positive conditioned stimulus is absent the theta rhythm of a reliably lower frequency is dominant in the potentials of the investigated brain formations (Efremova et al., 1981).

Therefore, the conditioned stimulus acts as a trigger setting off a series of systems, among them the system producing synchronized processes (theta rhythm) in the cerebral structures that reflect a certain degree of the latter's excitability and the system responsible for a uniform time flow of the bioelectrical processes in these structures (the system of spatial synchronization). The process is quite clear cut in the theta-rhythm range.

What are, then, the formations associated with control of the integration-disintegration of brain structures?

Data of the analysis show (Efremova et al., 1981) that in the inhibition states the theta rhythm persists in three of the four brain structures analysed (in the potentials of the sensomotor cortex, dorsal hippocampus, and anteroventral thalamic nucleus). For all that, its frequency (4.5 to 5.0 Hz) was significantly lower in comparison with the active state (6.0 Hz) in the realization of the conditioned reflex. By contrast, in the potentials of the mid-brain reticular formation the theta rhythm was observed reliably rarer than in the background or in the execution of the conditioned behavioural movement in response to CS application (Table 6.5).

The literature offers indications that the midbrain RF promotes increasing synchronism of the bioelectrical processes between different brain regions.

In experiments on rabbits short (one msec) single electrical RF stimulations were shown to elicit, in the brain cortex, particularly its sensomotor and visual regions, evoked responses that are much alike in their form. Synchronism of their occurrence

**Table 6.5.** Presence of 6-Rhythm in RF Potentials in Different Behavioural Situations

No of situation	Situation	Presence of behavioural reaction (paw flexion)	Presence of theta rhythm, %%
1	CS	+	100
2	Background before CS (+)	+	67.9
3	CS	—	81.3
4	Background before CS (—)	—	54.2
5	DS	—	58.0

becomes most clearly evident for the duration of 500 msec (Yakupova and Ignatiev, 1977).

The evoked responses to light with no RF stimulation in the same cortical regions appear to be much less similar.

The synchronizing effect of the midbrain RF is distinctly shown also if one collates the coherence functions immediately before and after the stimulation. Its level has been found to rise markedly between those two events as a result of short RF stimulation.

In experiments on rabbits a 10-second stimulation of the midbrain RF (100 and 250 Hz) was shown to increase the total summary synchronization level of the neocortex biopotentials in the range from 1 to 30 Hz sustained over 10 minutes and longer, and to add prominence to the theta rhythm and increase the level of coherence in the theta range between the potentials of the visual and sensomotor regions (Yanson and Markin, 1977).

Therefore, the excitation of the midbrain RF leads to an increasing level of spatial synchronization in the brain cortex biopotentials, thus presumably contributing to the functional interaction of brain structures in a certain activity.

The latter point is well illustrated by the data suggesting that evoked potentials in the visual and sensomotor rabbit cortex show greater similarity when a flash is delivered on traces of the previous RF stimulation (Yakupova and Ignatiev, 1977).

As shown earlier for automated controlled experiments, the spatial synchronization and coherent pattern of the processes in the theta range in the cortical potentials is a requisite condition for the spread of excitation between the respective analysers (Livanov, 1972; Korolkova, 1977).

This fact makes it possible to explain the activating effect of the midbrain RF. Obviously, it contributes to the spatial synchronization of the cortical bioelectrical processes and thereby encourages functional interaction between the brain structures involved. Such an influence of the midbrain RF was shown earlier

(Yanson and Markin, 1977) to engage much of the neocortex. But because the action of the exteroceptive stimulus (light) makes for the isorhythmical flow of the processes in the theta range both between different subcortical brain structures and the latter and the neocortex (Efremova et al 1979) and because of the sheer presence of numerous morphological connexions between the various brain formations, one may well hypothesize the spread of the RF influence not only on the cortical, but also on other, subcortical, brain structures.

Thus, spatial synchronism of the cortex potentials rises significantly with the accomplishment of an orienting reaction on exposure to exteroceptive stimuli. It becomes confidently higher also in conditioning (Efremova and Trush, 1971; Livanov, 1972; Luchkova, 1973).

In the experiments on rabbits for producing a conditioned defensive reflex to a non-rhythmical light reinforced with an electrical shock applied to the hind paw skin, a 'correlation field' of the brain cortex potentials was registered (Luchkova, 1973). In that case, one electrode, 'main' one, was posted on the skull bone, overlying the motor centre of the hind paw, and the remaining 23 electrodes were arranged in semicircumference at equal distances from it. Cross-correlation coefficients were then estimated between the 'main' centre and all other leads (Fig. 6.3) for the epoch of analysis equal to 1.5 sec. In magnitude, they conformed to the length of rays in the semicircumference. In this way the broken line joining the resultant points reflects the degree of synchronous (with the process at the 'main' point) occurrence of potential flow within the area of one hemisphere.

To see the significance of the correlation field from such an angle would be impossible, were it not for the findings of several studies elucidating the structure of spatial synchronization of rabbit cortex potentials (Tishaninova, 1974; Korolkova, 1977). The studies demonstrated that the cross-correlation coefficients of the rabbit neocortex potentials decreased monotonously with increasing distance between the electrodes leading electrical activity.

It is on these grounds that, by recording the cross-correlation coefficients between the potentials led from the 'main' site, on the one hand, and each of the leading electrodes, semicircumferent and equidistant from the latter, on the other, we are in a position to judge the level of the 'correlation field' in the neocortex.

So, with development of a conditioned defensive reflex the correlation field evenly spreads itself by degrees to all of the registered cortex areas (Luchkova, 1973) (Fig. 6.3).

Increasing general synchronization of the cortex potentials in elaboration of a conditioned defensive reflex in the rabbit stands out clearly from a review of histograms devoted to the distribution of

cross-correlation coefficients between the potentials of the sensorimotor and visual regions in the rabbit neocortex in the course of a conditioned reflex formation (Fig. 6.4). As is seen, progressing

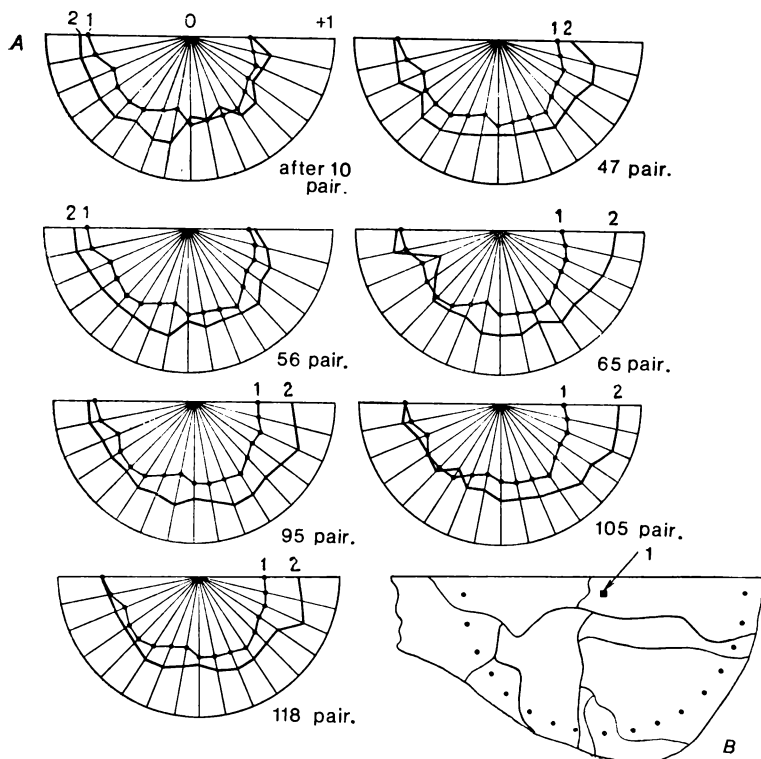


Fig. 6.3. A. Change of spatial synchronization between cortical potentials with the development of conditioned reflex to light. The graphs are in polar coordinates with the cross-correlation coefficients (C) between the motor centre and plots located around it at equal angles of  $11.3^\circ$ .

1—plotted on each ray are the values of C from 0 to +1.1, averaged background prior to the reflex development; 2—after a specified number of pairings.

B. Given on a schematic brain contour is the position of lead electrodes:

1—motor centre; the points denote remaining electrodes sitting on the radii at equal distances from it and at equal angles; the lines show the borders of Rose's cytoarchitectonic fields (Rose, 1931).

of the conditioned reflex formation causes the distribution maximum to shift towards the higher values of the cross-correlation coefficients (Luchkova, 1973[b]).

Yet, on the background of global enhancement of synchronization in the course of the conditioned reflex elaboration its preponderant

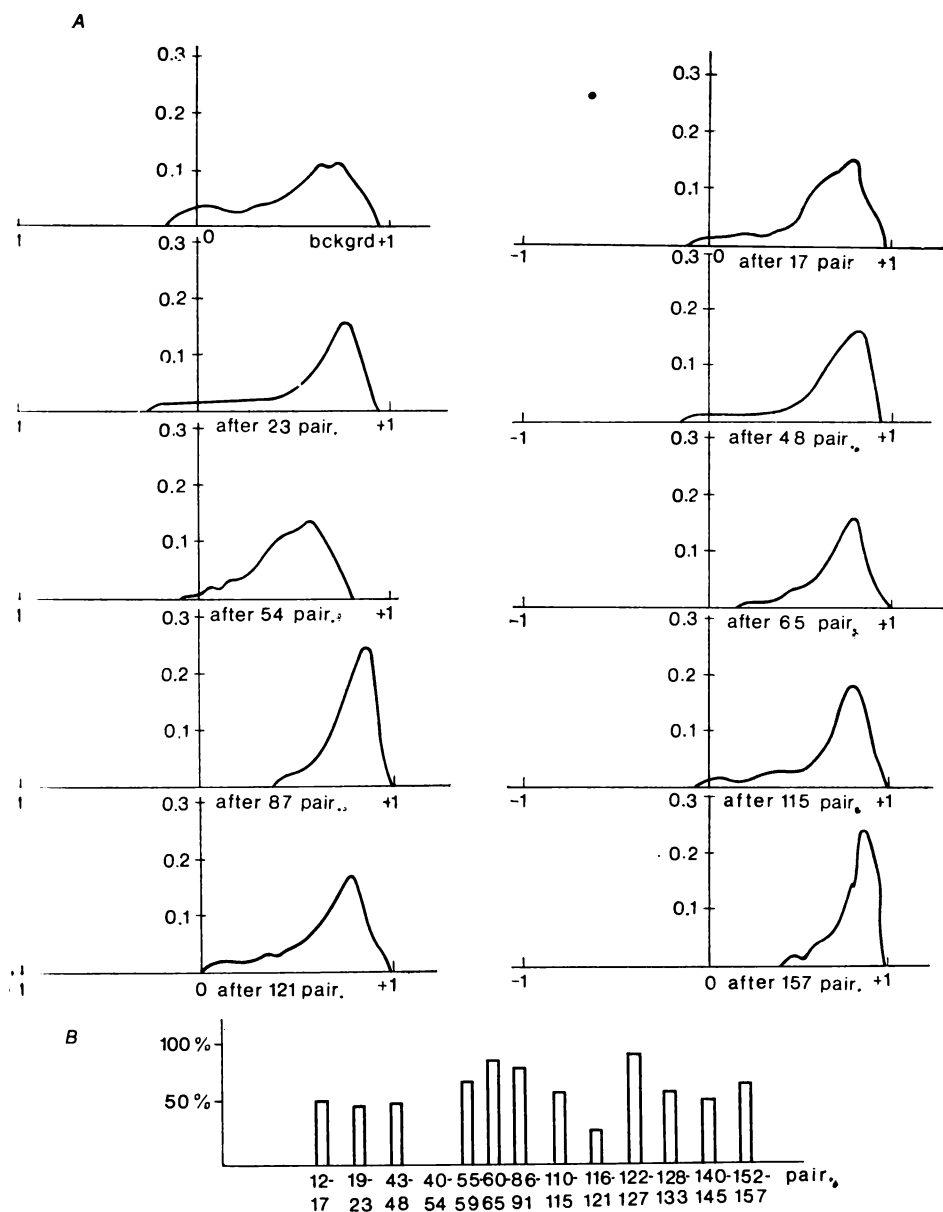


Fig. 6.4. Dynamics of change of distribution curves of cross-correlation coefficients in the development of conditioned defensive reflex (A) and diagram of motor conditioned movements (B).

growth was detected between the potentials of the 'concerned' analysers, i.e. the sensomotor and visual regions, in the development of the conditioned reflex to light reinforced by an electrical shock applied to the paw skin. This selective enhancement of synchronization comes on with particular clarity during the realization of a conditioned motor response (Luchkova, 1973[a, b]) (Fig. 6.3 and 6.5).

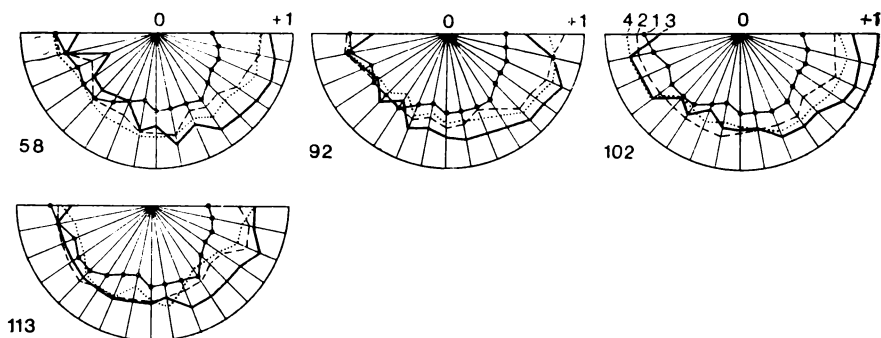


Fig. 6.5. Change of spatial synchronization of cortical potentials at the moment of action of conditioned stimulus with conditioned movements. The graphs are in polar coordinates.

— — — averaged background prior to conditioning; — — — averaged background at the action of conditioned stimulus; . . . immediately before action of conditioned stimulus (1.5 seconds before).

It is interesting to note that, in extinction, i.e. on exposure to a non-reinforced stimulus (light), and provided no conditioned movement takes place, no specific gain in synchronism of the potentials between the 'concerned' regions of the cortical analysers comes about either (Luchkova, 1973[b]).

As was shown earlier (Livanov, 1972), the magnitude of the cross-correlation coefficients between the potentials of rabbit brain structures depends mainly (with the exception of some states, in particular in differential inhibition) (Efremova and Trush, 1973) on the coherence level of the processes going on in the theta range.

It has been already said, nevertheless, that in conditioned defence reflex elaboration (to light, with an electrical skin reinforcer) the theta range owns broad scope also in cortex areas other than those of the 'concerned'—visual and sensomotor—analysers (Efremova and Trush, 1973).

In light of the fact that the cross-correlation coefficients represent a summary parameter and reflect the correlation of bioelectrical processes within a broad frequency range, it is not unlikely that the specific gain in synchronization between the potentials of the 'concerned' analysers in the realization period of a behavioural

conditioned act may be traced to a higher-frequency (above the theta band) area in the EEG spectrum.

Electrophysiological literature knows of relatively few works addressed to the EEG high-frequency components. One of the first to appear was a pioneer study on fast oscillations in human brain (Spilberg, 1947). It was followed in the 1940's and 1950's by a series of similar studies on different animals and with visual EEG analysis as the basic research tool. Their authors were then in disagreement about the origin of high-frequency EEG rhythms, suggesting, among others, the 50 Hz range for them. Other workers attributed it to the vibration of conchae in rabbits (Khechinashvili and Roitbak, 1950) and still others favoured strongly a neural nature for the rhythm but related it to the activity of the olfactory analyser alone (Khvoles and Novikova, 1948; Novikova and Khvoles, 1953).

But even in those years, at least some of the studies then published (Gedevanishvili, 1948, 1955) succeeded in locating the origin of the 55 Hz rhythm in rabbit EEG both in the olfactory bulb and the frontal areas of the neocortical frontal lobe on exposure to various exteroceptive stimulations which induced an animal's alertness or emotional arousal.

On the contrary, with the animal fully at rest and with no external stimuli to attract his attention, the rhythm would be reduced.

In conditioning in a rabbit this author discovered that the 55 Hz rhythm had increased markedly and emerged no longer in the form of separate bursts and spindles, as in the orienting reaction, but manifested itself continuously, with a large amplitude, and not only in the EEG of the frontal brain regions but also in the visual area of the neocortex (in the development of a conditioned reflex to light) (Gedevanishvili, 1948).

A number of researchers, while not denying the origin of such rhythms in the olfactory brain structures in connexion with respiration, referred to influences by other possible brain formations on these structures (Hernandez-Peon, 1960; Brooks, 1962; Pagano, 1966).

It was argued in this context that the rhythms from 40 to 70 Hz may indicate the functional state of the brain. Hernandez-Peon (1960) and Pagano (1966) offered direct evidence for amplitude changing of the high-frequency EEG components of the olfactory bulb (in the range of 50 to 100 Hz) in cats in response to electrical stimulation of the midbrain reticular formation.

Though the above-enumerated works did prove the neural nature of the EEG high-frequency components, nevertheless their authors had been unable to ignore the influence of respiration upon this activity.

By the method of EEG recording in a tracheotomized animal with air-blowing in rigorously measured quantities through the nasal passages (Schwartz, 1970[a, b]), it had been possible to exclude the factor of influence of nasal respiration on EEG rhythms and thereby directly prove the amplitude of the high-frequency EEG components of the olfactory brain to be dependent upon influences of other various subcortical formations when electrically stimulated and also when exteroceptive stimuli were presented to the test animal.

In this way, the influence on the high-frequency activity of the olfactory brain by other structures was firmly established, and so was the fact that the high-frequency EEG components of the olfactory brain could reflect the functional state of the brain.

Whereas a majority of contributions to the research on the high-frequency EEG components were executed on the olfactory brain, some were concerned with other brain formations.

One such, by Pickenhain and Klingberg (1969), showed the existence of high-frequency activity for the neocortical (sensorimotor and visual regions), and dorsal-hippocampal regions independent of the similar activity by the olfactory brain.

In experiments on unanaesthetized rabbits (Stumpf, 1965) and cats (Bradly, 1962; Boudreau and Freeman, 1963) the existence of the hippocampal high-frequency activity was documented in the 40-70 Hz range, at once with a somewhat slower theta-range activity. The authors' conclusion was for independent origination mechanisms of these two types of rhythmical activity.

Several authors took notice of the high-frequency rhythms (60-70 Hz) in the EEG of the rabbit sensorimotor cortex that appeared during instrumental conditioning (Sadowski and Longo, 1962) and in different areas of the dog neocortex (30-35 Hz)—during defensive conditioning (Lurie et al., 1956), or in a stereotype of conditioned reflexes (Sakhiulina, 1955).

In conclusion, the literary facts cited above with respect to EEG activity in the 40-70 Hz range indicate it to be of the neural nature, inherent in the olfactory as also in other brain structures, and varying in character with the functional state change of the central nervous system, because it reflects, presumably, the latter's active state. The origination mechanism of the high-frequency activity is probably different from that of rhythms in a more slow range, theta rhythm for one (Stumpf, 1965).

In recent years, high-frequency components of the biopotentials of rabbit neocortical and dorsal-hippocampal regions have been studied in our laboratory with the Fourier fast-transform method on an EC-1020 computer.

The findings revealed the presence, in spectrograms of investigated cerebral regions, of a dominant frequency in the region of



50 Hz, during elaboration of conditioned defence reflex in rabbit to non-rhythmical light reinforced with a shock applied to the paw. An analysis of the coherence functions between the potentials of the brain areas being studied identified, at the stabilized conditioned reflex stage, a high level of coherence in the narrow range around 50 Hz, selectively between the potentials of the 'concerned' analysers (i.e. the visual and sensomotor neocortical areas) to which the conditioned and unconditioned stimuli had been addressed. Between the biopotentials of the regions unaddressed by the conditioned and unconditioned stimuli (i.e. between the auditory and sensomotor regions) the coherence level was significantly lower (Efremova et al., 1981).

Dumenko (1977) called attention to the functional role of the high-frequency components of the neocortical potentials in dog in conditioning food-acquisition and defensive reflexes.

One would gather the impression as if theta rhythm, the basis of spatial synchronization between numerous cortical and subcortical structures, were spreading globally through these structures in parallel with the formation and realization of the conditioned defence reflex. It is therefore not surprising that, to judge by this one parameter (theta rhythm), many cortical and subcortical structures seem to contribute to the formation of conditioned reflex. For the findings of many-year research by numerous authors have built a convincing case for the principle of integral brain activity underlying its actual operation (Belenkov, 1980).

The principle does not rule out, however, predominant activation, in different functional states, of appropriate brain structures.

Indeed, studies on rabbits by a variety of methods—isolation of neocortex from the subcortical formations by Khananishvili's method (Khananishvili, 1971); cross-cuts setting apart its different structures; and isolated cortical strip by Burns' method (Burns, 1950)—showed the existence of a well-defined architecture of spatial synchronization between brain cortex potentials in the background. It reveals itself through monotonously decreasing values of cross-correlation coefficients with increasing distance between the lead electrodes and is contributed to by both, intra-cortical as well as subcortical-cortical influences (Tishaninova, 1974; Knipst, 1967, 1976).

As previously mentioned, there are reasons to believe that global synchronism enhancement of the cortical potentials in conditioning has to do with the diffuse influence of the reticulo-septal system (Livanov, 1981).

In actual fact, the more local, specific gain in synchronism mentioned earlier between the cortical potentials of the 'concerned' analysers does not appear in response to the presentation of conditioned stimulus under the conditions of temporary blocking out

by novocaine or dc-anode, of mamillary bodies or non-specific nuclei in the thalamus (midline nuclei or interlaminar nuclei), along with some nuclei in the hypothalamus (posterior or dorso-medial nuclei). As this happens, the conditioned behavioural reaction does not occur either, whereas the global synchronism of the cortical potentials persists as before (Luchkova, 1979) (Figs. 6.6 and 6.7).

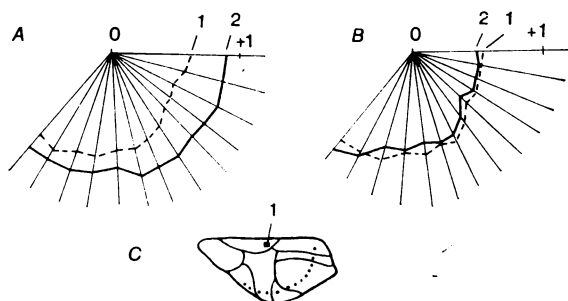


Fig. 6.6. Change of spatial synchronization between cortical potentials under temporary blockade of n. mammillaris medialis during action of conditioned stimulus.

Rabbit No 61. 1—averaged background just before action of conditioned stimulus; 2—at the moment of its action. A—prior to polarization: the 140 pairings—with movement; B—at the time of polarization: the 142 pairings—with no movement; C—position of the electrodes in a schematic contour.

Therefore, there is enough evidence to postulate a major role of the just cited subcortical formations, i.e. non-specific thalamic nuclei, some hypothalamic nuclei and structures of the limbic circle, in the initiation of the 'specific' synchronization between cortical potentials as conditioned reflex is realized.

The fact that some rhythmical EEG components of a rabbit's neocortex depend on subcortical influences was illustrated in a study with potentials registration from an isolated cortex strip (Elkina, 1975; Bobkova, 1979).

A spectral analysis of the EEG of an isolated cortex strip under these conditions indicated that theta-rhythm oscillations in the neocortex also took place when the latter was isolated against influences by subcortical centres and other brain formations, particularly dorsal hippocampus. For all this, the theta rhythm of an isolated neocortex strip differs in frequency from the theta rhythm of other brain formations and the level of coherence function between the processes proves to be low.

The facts discussed above confirm the involvement of cortical-subcortical processes in the production of cortical rhythms and the

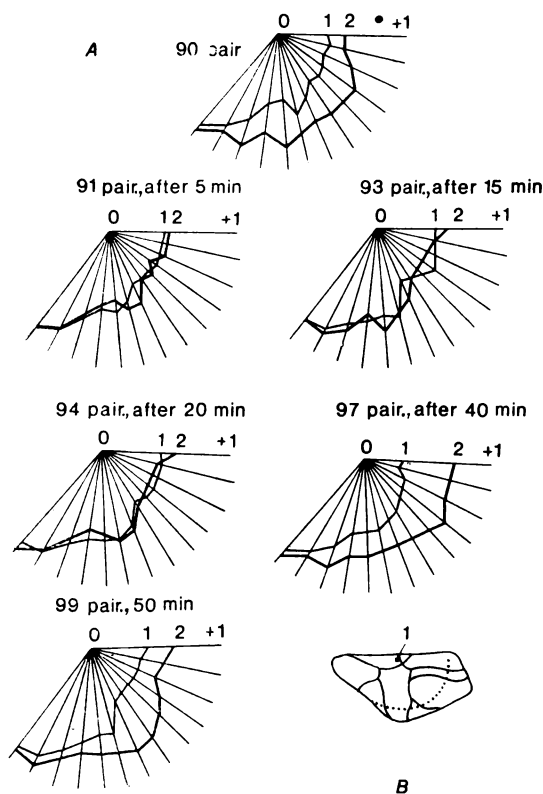


Fig. 6.7. Change of spatial synchronization of cortical potentials in the development of conditioned reflex with temporary blockade of non-specific thalamic nucleus (n. reuniens) by anodic polarization. Rabbit No. 50.

A—the graphs are in polar coordinates, with C values from 0 to +1 plotted on each ray. 1—averaged (for 32 C) background in the intersignal period immediately before the pairing; 2—at the moment of action of conditioned stimulus (1.5 sec. epoch); prior to polarization: the 90 pairings; during polarization: the 91 pairings after 5 minutes; the 93 pairings after 15 minutes, and the 94 pairings after 20 minutes; upon termination of polarization: the 97 pairings after 40 minutes; the 99 pairings after 50 minutes; 90, 97 and 99 pairings—with movement; the 91, 93, 94 pairings—with no movement. B—given in a schematic contour of brain is the position of electrodes.

architecture of cortical spatial synchronization and, consequently, in conditioning and in conditioned reflexes realization.

Analysis of the results obtained lends credence to the assertion that there are two systems in control of cortical activity, not least in conditioning and in realization of conditioned reflex. One of these acts diffusely (reticular-septal) and another one (mamillary-

thalamic) exerts a more local influence on the cortex. Interaction between the two systems turns out to be a necessary condition for the formation and realization of conditioned reflex.

In view of the facts cited in the foregoing, one may suggest a greater role for the high-range frequencies in the activation of the second system.

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# 7

## The Dominant and Its Role in Animal Behaviour

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The first observation of the dominant we find in the work of the Russian physiologist Wedensky (1951[a]). In 1881 he studied the influence of electrical stimulation of the vagus nerve on breathing movements of the animal. In the course of this research he discovered that, when the excitation of the nucleus of the vagus nerve was increased by long stimulation, the addition of short stimulation of other sensory nerves had the same effect on respiration that it would if the vagus nerve itself were stimulated.

Wedensky (1951[b]) observed the similar phenomenon of the dominant in a different experiment. Certain points in the motor cortex were stimulated for some time. This was shortly followed by stimulation of other cortical areas and the effect obtained was of the type common for the previously stimulated point. At the time, these findings were considered by Wedensky as 'distortion' of the reactions involved—when some stimulation provokes quite another reaction than that ordinarily elicited by the stimulus.

In 1904 Ukhtomsky (1966), while preparing a dog for one of Wedensky's experiments with stimulation of the motor cortex, was astounded to see the contents of the animal's rectum thrown out in response to a stimulation of the cortex that would normally yield the movement of the forelimbs. When the act of defaecation would draw to a close, increased excitability would be observed at the cortical points connected with the limb movement. Uncertain just then about the physiological implications of the occurrence, Ukhtomsky jotted it down 'for memory' and in 1909 proceeded with its experimental investigation. The result was a dissertation 'On the Dependence of Cortical Motor Effects upon Collateral Central Influences' (*Ibid*, p. 31).

In 1923-1927, in a series of works, Ukhtomsky outlined the key concepts of his theory concerning the dominant. The dominant was held to be a general principle in the action of nerve centers; it underlies the constant reorganization of intercentral relations. The application of the dominant principle was described by Ukhtomsky in the biological, philosophical and behavioural aspects.

Ukhtomsky defined the dominant as follows: 'A prevalent focus of excitation that predetermines in large measure the character of

ongoing central reactions at a given moment' (Ukhtomsky, 1950, p. 164).

... 'a stable focus of increased excitability of centers, however it may be caused, getting the excitations newly arriving at the centres to augment (reaffirm) the excitations in the focus, with inhibition broadly diffused elsewhere in the central nervous system' (*Ibid*, p. 165).

... 'partly under the influence of hormones of the organism and partly under the reflex influence from outside, foci of increased excitability develop in the nervous system, which, precisely because of their increased excitability, show somewhat facile responses to most diverse and distant stimulations applied to the organism' (*Ibid*, p. 186).

Further on: 'a sufficiently steady excitation... accumulates within it the excitations from most distant sources but inhibits the ability of other centres to respond to the impulses directly relevant to them' (*Ibid*, p. 190). And the last of his definitions of the dominant, to be found in the entry he wrote for the first edition of the *Large Soviet Encyclopaedia*, said: 'the dominant (L. *dominans* ruling) in physiology is a temporarily dominant reflex by which the operation of other reflex arcs and the reflex apparatus as a whole is transformed and guided in a given time, other conditions being equal' (*Ibid*, p. 325).

Summing up the characteristics of the dominant Ukhtomsky concluded on the dominant to be characterized essentially by increased excitability, persistence of excitation, summation and inertia. One must not overlook Ukhtomsky's emphasis on a certain level of increased excitability necessary to produce the dominant. An excessive increase of excitability beyond that level renders the focus of excitation incapable of further summation. It was summation Ukhtomsky conceived of as the major property of the dominant. He wrote, 'One would be extremely careless to presume that the dominant is "the centre of strong excitation" in the sense of some stationary state. To be precise, all one needs to say is that the dominant is the centre most readily responsive to distant waves and very easily summing in itself the excitations caused by them' (*Ibid*, p. 281).

Ukhtomsky spelled out the basic substantive assumptions regarding the dominant. Yet many aspects in the expression of the dominant, such as the possibility for several dominants to co-exist in the central nervous system (CNS), selectivity of the receptive field of each dominant, the neurophysiological essence of summation, reciprocal inhibition, and the role of the dominant in animal behaviour need further experimental research.

Close examination of Ukhtomsky's work approaching the dominant as the supreme reflex act inhibiting all other activity gives



the impression as though only one dominant focus could exist in the CNS at any given moment. In reality, however, these relations have proved to be more complex. Subthreshold stimulation of the rabbit limb is able to establish in the CNS a dominant focus identifiable upon application of a sound stimulus; a similar focus can be set up by subthreshold stimulation of the eyelid muscle that makes a rabbit blink in response to the sound. It turned out that, when such subthreshold stimulations are delivered simultaneously to the paw and the eyelid muscle, the rabbit moves the paw and blinks in response to the sound. Facts indicate that when two dominant foci are initiated, as in the given case, they can exist both at a time.

The possibility of simultaneous existence of two dominant foci is apparently determined by the fact: in what central apparatuses dominant foci are produced, and what are functionally fixated relations between these centres. Indeed, the rabbit was shown to be able to move the paw and blink simultaneously. In the first of the instances observed by Ukhtomsky the defaecation at the time of limb movement was not a natural form of the dog's behaviour. Probably the dominant state in the blinking reflex centres can exist simultaneously with the similar states in the central apparatus of the swallowing reflex as well as in numerous other reflexes functionally compatible with the blinking reflex.

It is hard to imagine why, with the increasing tonus of the nucleus of the vagus nerve and with the added stimulation of another sensory nerve (as in Wedensky's, 1951[a], experiments) having the same effect on respiration as does the stimulation of the vagus nerve no other reflex activity can conceivably be effected on the dominant principle, e.g. in the motor analyser?

One is well familiar with what is called in the literature *locus minoris resistencie*—when a short-time disturbance in the activity of a particular internal organ provokes a painful sensation in a man not in this organ, but in another one affected by chronic disease. Can't one concede, then, in the interaction based on the dominant principle between the centres innervating the internal organs, the simultaneous existence of some other activity, likewise patterned on the dominant principle?

An example will be in order from higher nervous activity in man. In the state of a creative dominant a person relating his thoughts on paper notices nothing around him. As problems arise he lifts his head and gets to thinking. When he is just about to proceed with his work, he finds his hand to be no longer holding the pen but massaging the chest in the heart area. Later he becomes conscious of painful sensations in his heart and recognizes them to be the ones that have produced the reaction. This second dominant occurring on the subconscious level recalls in

some ways Ukhtomsky's model (*Ibid.*, p. 191) when a frog, wherever it is stimulated, exhibits the scratch reflex of those skin areas which correspond with the poisoned spinal cord segments.

Another example from man's everyday life. Mothers know perfectly well that they can attain a level of training enabling them, even when possessed by some thoughts, to go on thinking about it while simultaneously reading a tale to the child. The mother does not hear her own voice, nor does the idea of what she is reading reach her mind, yet the subsequent questioning of the child shows that the reading process has been correct.

Analysis of many behavioural situations, as also of some physiological models, shows conclusively that in a normally functioning organism there must be inherent mechanisms allowing the co-existence of several dominants. This depends on those specific reflex acts which the dominants are connected with. When such biological motivations as feeding, defence or sexual ones compete with one another, one of them becomes dominant.

To draw a line on the foregoing discussion, dominants may be functionally compatible or incompatible. A closer review of CNS representations of specific reflexes suggests that potentially the incorporation of the centres into functionally compatible or incompatible dominants is dictated not by their proximate or distant locations relative to one another nor their anatomical topography, but rather by genetically fixated systems of functional linkages in the CNS. Within the systems, the interrelationships of the nervous centres follow the dominant principle.

Given a continuous inflow of impulsion, it is rather likely that several dominant foci will appear in the CNS all at a time. If the foci are parts of a system comprising functionally incompatible activities, supremacy for one among the foci comes as a result of power relationships between the dominant focus present and the one that appeared anew. In that case, the intercentral relationships are determined, in fact, by the 'power play' between the two dominants.

Another question of immediate concern in the context of possible simultaneous existence in the CNS of several dominant foci refers to reciprocal inhibition allied with the dominant. In his major publications on the subject of the dominant (1923-1927) Ukhtomsky would accentuate time and again the diffusive character of reciprocal inhibition that arises in the CNS as the dominant focus takes form. Speaking about summation in the dominant focus he made a special case for the 'inhibition broadly diffused elsewhere in the nervous system' (*Ibid.*, p. 165). The dominant focus 'inhibits the ability of other centres to respond to the impulses directly relevant to them' (*Ibid.*, p. 190).

Later (1937) Ukhtomsky sounded more cautious about that.

Rather he would speak about inhibition of reflexes functionally incompatible with the dominant, arguing that 'any central reaction can come into the position of dominance... just as any reaction might be in the state of conjugate inhibition, when this reaction is little compatible with the just prepared central activity' (Ukhtomsky, 1966).

Indeed it is hard to imagine that, whenever a dominant focus is initiated in a CNS area, all of its other centres are in the state of inhibition. In our joint study with Malikova (1978) a dominant was formed by multiple subthreshold stimulation of the rabbit forelimb. It was detected by electrical stimulation of the eyelid muscle which elicited the limb contraction but no inhibition of the blinking reflex.

The question arises, what processes in the CNS determine the inhibition of some reflexes under the dominant, and not of other ones? Clearly, this is not controlled by anatomical interaction between the effectors involved. Under the dominant reciprocal inhibition spreads to the central links of exclusively those reflexes which are functionally incompatible with the dominant focus.

When does reciprocal inhibition develop under the dominant, during or prior to the execution of the reflex involved? The available experimental evidence seems to favour stronger the notion that the subthreshold state of excitation, which may be designated as a dominant state, already exerts powerful reciprocal inhibition on definite central apparatuses, even though the activity that identifies the presence of the dominant is to come yet. Or, to recall the first observation of the dominant by Ukhtomsky, the threshold for evoking the limb movement is already heightened, while the summation which leads to a reflex is still missing.

Doing studies in animal conditioning Anokhin (1968) also paid attention to the likely existence of reciprocal inhibition in a dominant state unaccompanied by its adequate activity. When a dog with developed conditioned defence reflexes is placed in the experimental environment it will ordinarily react with inhibition to feeding conditioned stimuli though not jerking back the limb.

An experiment with urgent reinforcement of a conditioned signal with meat instead of habitual bread furnishes another revealing example. Reinforced with meat, the animal in subsequent experiments goes right from the beginning to the feeder that had once provided meat. The dog then would be sitting at the feeder with no visible signs of feeding excitation (secretion, respiration). However, when bread was given next the animal would not eat the food (Anokhin, 1934).

These examples demonstrate that the dominant state unexpressed as yet in outward activity, already inhibits another activity. It is not that summation in the dominant focus produces reciprocal in-

hibition. Rather conversely, a sufficiently strong excitation is attended with conjugate inhibition which spreads to the efferent portion of the reflex arc and thereby leads to a situation when its own excitation, as it meets the inhibition block, propagates itself via other paths and summates with the excitation present. This is to say, reciprocal inhibition acts primarily as the organizing agent of summation at the available excitatory focus.

The questions previously asked with regard to reciprocal inhibition under the dominant focus indicate that the mechanism underlying organization of this phenomenon and the neurophysiological essence of the process involved are not clear and require further experimental treatment.

Neither is quite clear the question about the afferentation potentiating the dominant focus. Comparison of the dominant foci initiated in different CNS regions may identify each one of them as having selective sensitivity to a certain set of stimuli. The dominant focus set up by the method of polarization in the sensorimotor cortex may be detected by exposure to various light, sound or tactile stimuli. But even so the focus is maximum sensitive to the tactile stimuli, rustle is most effective of the sound stimuli and light seldom leads to summation in the dominant focus. There is no doubt that the dominant focus produced in the CNS by stimulation of internal organs will be potentiated primarily by the afferentation coming from other internal organs, and not by distant stimuli.

In any motivated behaviour the dominant state in the appropriate centres is potentiated selectively by signals biologically meaningful to this particular form of behaviour. In this vein, tactile stimuli and rustle among the sound stimuli, are more meaningful to the rabbit defence dominant. The feeding dominant has a low threshold for olfactory signals. One finds quite interesting the data of Batuev et al. (1975) on selective responsiveness by neurons of the frontal cortex of a cat to sound stimuli with a frequency whose energy maximum occurs in a number of sound signals specific to the cat. Such selective sensitivity of specific central structures to certain stimuli is presumably based on genetically fixated connexions between different CNS regions.

Returning to the dominant, it must be stressed that despite its ability to be potentiated from a broad receptive field, its threshold of responsiveness varies with biologically meaningful or indifferent stimuli for a given dominant. This is due basically to inborn fixated connexions between different CNS regions. It appears there are certain CNS systems of interconnected centres which may stand in a dominant-subdominant relation to one another. Then reinforcement of the dominant focus comes through impulsion, principally, from certain CNS areas and not from the whole CNS.

Data on single neurons have shown that induced enhancement of the neurons' excitability with the increasing frequency of spike activity lowers the threshold of their response to many stimuli that previously failed to produce the reaction. Neurons in the motor cortex, to take one example, begin to show short-latency responses to light and sound stimuli (Brazovskaya et al., 1972). If one considers in addition interneuronal relationships as well as those between single neurons and neuroglia, it becomes clear that, combined together, they bring about the formation of a dominant focus (Brazovskaya et al., 1972; Pavlygina, 1972; Pavlygina and Rusinov, 1976). It seems that a goal-directed investigation of responses to different stimuli by individual groups of neurons in enhancement of their excitability will help reveal exactly what reflexes could be potentially involved into the intercentral relations based on the dominant principle.

Let us examine another aspect of Ukhtomsky's concept of the dominant. Ukhtomsky's interest concerning the organization and coordination of reflex acts is closely interwoven with the problem of determination of behaviour. In many of his works it is pointed out that the reflex which is dominant among the many possible reactions determines the direction of behaviour of the entire organism. Ukhtomsky argued, 'Every time there is the symptom complex of a dominant, there is also a vector of behaviour predetermined by it. Hence it is natural to call it the "organ of behaviour"...' (Ukhtomsky, 1950). And he goes on: 'The dominant is something more than just a normal operating principle for the centres—it plays essential role in the process of newly formed reactions to the environment' (*Ibid.*, p. 192).

The problem of motivation is seen in Ukhtomsky's work under a variety of aspects, among them physiological and psychological and so on. It should be noted that in his approach to the dominant as the source of goal-directed behaviour Ukhtomsky would invariably remain loyal to the reflex theory.

It would appear as if Ukhtomsky's entire theory of the dominant, when there is no permanent mechanism with a 'unique manner of action', were a breach of the traditional reflex scheme whereby stimulation of the receptor produces inevitably one and the same motor or secretory effect. Nevertheless, like Sechenov and Pavlov, Ukhtomsky averred that his conception of the dominant's role in behaviour basically did not disclaim the reflex theory but rather sought to specify the classical reflex scheme so as to integrate transformations in the central part of a whole reflex act. He came to the conclusion that the concept of dominant explains 'a great deal in the mysterious variability of reflex behaviour in humans and animals with imperceptibly little-changing surroundings' (*Ibid.*, p. 317).

That the very principle of behaviour predetermined exclusively by inborn drives was unacceptable to Ukhtomsky, is clearly evident from the attitude he embraced in the discussion about instincts. At that time, instincts were seen by many as the regulation of action in accordance with goal. 'With some seven instincts on hand we shall not be able to make sense of specific behavioural acts' (*Ibid.*, p. 308). 'It is best of all perhaps to follow I. P. Pavlov's lead in his report in America where, with so much tact, he simply would not raise the question about instincts as such, apart from reflexes, but say instead "instinct, or reflex". True enough, the concept of instincts includes nothing else but the reflex' (*Ibid.*, p. 309).

In this way, Ukhtomsky's view of the dominant as the principle of intercentral interaction led him to infer that the supreme (dominant) reflex underlies the 'motivational' leverage of animal behaviour. In his conceptions of the dominant Ukhtomsky approximated very closely the problem of behavioural motivation.

At present numerous authors agree that the mechanism of the dominant participates in the organization of motivational behaviour in animals. Anokhin (1968) insisted on involvement of the dominant mechanism in certain stages of behaviour which he called the stage of 'afferent synthesis' and applied to it the psychological term 'decision-making'. Sudakov (1971) shares this view and by now the expression 'dominant biological motivation' has become widely popular.

Besides this term, the literature devoted to the research into animal motivational behaviour offers a wealth of experimental data suggesting that, whenever this or other motivated state is initiated, the respective central structures possess the properties of the dominant.

Indeed, Khayutin (1973) disclosed numeric growth of the visual cortex neurons responsive to light flashes with naturally increased feeding motivation or with stimulation of the 'hunger centres' in the hypothalamus. Sinichkin (1979) pointed to enhanced convergence of cortical neurons following stimulation of the motivational centres in the hypothalamus.

Sosnovsky (1979) and Lisitsky (1979) found the converging properties of neurons in the frontal regions of the rabbit cortex to add intensity on exposure to electrical stimulation of the 'hunger centre'. Responses to light and sound were emergent, the cells reacting to individual stimuli increased in number and the quantity of polysensory cells multiplied in rabbits in the state of hunger, according to Belenkov (1979).

McClelland et al. (1949) showed that a hungry man conceives of indefinite or false stimuli as being associated with food. Hinde in his book *Animal Behaviour* (1970) provides evidence to prove

that strengthened motivation rather heightens the reactivity to stimuli than potentiates motor activity. In an impoverished environment hunger-stimulated activity in rats grew by 10 per cent, and by 400 per cent in an enriched environment.

Simonov (1979) analysed efficiency of man in recognition of visual images with increasing emotional strain imposed on him by a forthcoming parachute jump. It turned out that many events in

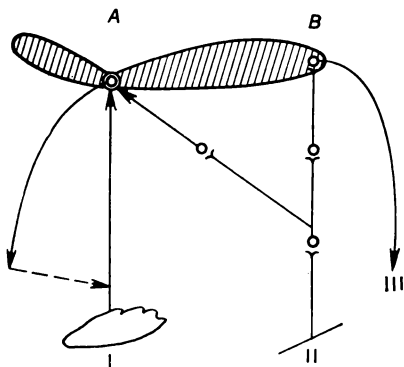


Fig. 7.1. Dominant-based organization of animal goal-directed reaction.

A—dominant focus in the central nervous system; B—central link of unconditioned reflex; I—receptive field of dominant focus; II—afferent arc of the unconditioned reflex; III—efferent arc of the unconditioned reflex. For the explanations, see the text.

the external environment became meaningful to the subject—the effect described by the author as increased responsiveness on the dominant principle.

Thus, a large body of factual evidence on the dominant, whether or not it is actually mentioned by the authors, is available today—enough to postulate that its attributes are present in motivational behaviour of animals and humans.

Let us examine, with a recourse to our knowledge about the dominant, the ways in which the dominant comes to realize goal-directed behaviour in animals.

For ease of perception, we shall provide the following scheme (Fig. 7.1). The central apparatuses A are in the dominant state. The dominant receptive field may be determined by both, the stimuli, coming in from the external environment, and by excitation of receptors in the circulatory system, or hormonal changes in the body, i.e. all those readjustments in the internal environment which are undoubtedly connected with an upset balance with the external environment. It is therefore not necessary to distinguish in principle between information inputs from outside the body and from the internal bodily medium.

When a certain level of excitation has been achieved in the central structures of a given reflex (A) the excitation passes to the effector. When does, then, the dominant state arise in the centres? Repetitive activation of the receptive field yields stable excitation at site A, accompanied by reciprocal inhibition. The latter does not capture all of the CNS areas adjacent to centre A, but only the centres of functionally incompatible activity (shaded fields in Fig. 7.1).

Asratyan (1955) introduced a new scheme for the functional architectonics of unconditioned reflex. It depicts unconditioned reflex as being not unilinear, nor passing through just one CNS portion, but comprising many levels and branches each of which passes through one of the more essential levels in the system. Keeping this in mind, the course of events under the dominant may be visualized as follows. As a stable focus of excitation comes up in centre A the reciprocal inhibition extends to some, but not all, levels of unconditioned reflex B. When it embraces the upper levels of the reflex arc it thereby produces a block for transmission of the afferent volley to the efferent arc segment. Yet the afferent flow from the receptive field of reflex B continues to come on. Since the principal path is blocked, the impulsation flow along the lateral paths increases.

With inhibition of the efferent arc of reflex B, the excitation flowing along the side branches and perhaps through the same reticular formation is enhanced and, as soon as it reaches centre A, summated with the excitation focus there. As the result of the summation at point A the subthreshold focus of excitation reaches the threshold value and comes up to the effector.

It is worth noting specially, in regard of the proposed diagram for the interaction between the two centres that follows the dominant pattern, the active role of reciprocal inhibition in making the summation in the dominant focus a highly organized process.

Ukhtomsky distinguished four major features in the dominant: increased excitability, persistent excitation, summation, and inertia. The conjugate inhibition associated with the dominant was seen by him more as a result of the dominant activity than as an obligatory element necessary to perform the summation. In terms of the diagram above, the processes under the dominant follow the sequence: persistent excitation having its definite optimum excitability, reciprocal inhibition, and summation.

When the dominant becomes revealed through a functionally compatible activity, summation occurs without inhibition of this activity. Our data (Pavlygina and Malikova, 1978) have shown that, moreover, the central apparatus bound up with an activity functionally compatible with the dominant present is in the state of increased excitability. For instance, in defining a defence domi-



nant by the blinking reflex the latter is even enlarged in amplitude, even though the parameters of the current stimulating the eyelid remain unchanged. The centres' excitability increases most probably because of inductive intercentral relationships—when inhibition of some CNS areas raises the excitability of other areas. From Fig. 7.1 it is readily apparent that conjugate inhibition under the dominant is not diffusive in character but spreading in the CNS as 'tentacles' (shaded plots). The intermediate areas possess increased excitability and activation of these CNS areas begins to amplify the already available CNS excitation focus.

In conclusion, whenever a persistent excitation focus of the predominant type takes form in a particular CNS area, the result includes a mosaical change in the functional state of other centres, conjugate inhibition of some central apparatuses and inductive excitation of other ones. Here, too, conjugate inhibition provides a necessary link for organizing the summation. The presence of the inhibition process in a specific situation enhances the impulsion flow from distant CNS areas to the available focus of persistent excitation, and summation ensues.

Subsequent to the question 'how does it happen?' it is desirable to ask next: what about its biological significance?

Presumably, with a continuous impulsion inflow from the receptive field, the centre A excitation could well achieve the threshold value without any summation inputs from 'other sources'. The biological significance of the dominant lies not merely in having other activity inhibited and the supreme activity enhanced. It springs also from the fact that, owing to the summation mechanism, this activity comes earlier than it would if the centre's potentiation came from the receptive field only. In feeding motivation of animals 'the hungry blood' brings up the proper centres to a level sufficient to trigger a chain of behavioural acts to supply the given need. But because the motivational centres find themselves in the dominant state and summate the excitations from other sources, the threshold level for a behavioural reaction is achieved earlier, so that the animal has more time for food searching.

Assuming, that in the given example the motivated behaviour of an animal were organized without the dominant mechanism, with nothing to induce it but the 'hungry blood' alone, this behaviour is likely to appear when the animal's time is too short to do something about his need—and then irreversible changes will occur in its organism.

The importance of the fast accomplishment of dominant activity may be examined from two aspects. On the one hand, additional impulsion inflow to the CNS, besides that creating a dominant focus, may signify the necessity for a new activity. If so, the fast accomplishment, by virtue of the dominant mechanism, of the

supreme activity in a given moment at the expense of the 'added' impulsation will be helpful in faster including into the subsequent activity. More so because the excitability in the reciprocal centres increases once the inhibition state has gone by, and they promptly engage in the activity.

On the other hand, the fast realization of the dominant activity is essential for animal adaptive behaviour. A reminder is in place here that specific dominants are endowed with selective sensitivity to definite stimuli. This means that the level of excitation at the dominant focus is contingent not only upon the activation of the dominant's receptive field, but also upon the availability of a certain set of the impulsation inputs arriving via afferentation from outside.

Accordingly, the readjustments in progress in the interior milieu of the body are not the only determinant of the dominant state underlying animal motivated behaviour. It matters also what changes occur in the external environment and what set of stimuli dominates in that environment at a given moment. Early realization of a particular activity on the dominant principle implies, first and foremost, adequate reactions to environmental changes. Our treatment of the dominant in the behavioural aspect seeks to emphasize, therefore, its biological significance as a means employed by the adaptive and protective mechanism to exert its action.

We have thus far examined the dominant in the neurophysiological and biological aspects as it exists on the summation stage. What are further manifestations of the dominant after the summation stage, and what possible role does it play in organizing goal-directed reactions of the organism?

Ukhtomsky pointed out that the reflex act which results from summation brings the dominant to an end, or to 'solution'. He made a distinction between two possible solutions of the dominant: exogenous and endogenous (Ukhtomsky, 1950, p. 192, 199). To the former, he referred a case of inhibition of the dominant already present by a newly emergent one, but beyond that 'a persistent reinforced excitation of the centre is able by itself to prepare the inhibition process' (*Ibid.*, p. 192). The understanding of the endogenous dominant solution by Ukhtomsky meant fairly precisely a chain reflex directed at a certain act of resolution which terminated the dominant.

Faced with an uninterrupted impulsation inflow from the dominant receptive field, as in the former case, one can expect its termination to be only temporary and its subsequent, postinhibition reappearance not all that unlikely. It is therefore assumed that the true termination of the dominant can occur in the situation classified as endogenous.

Let us review in more detail the course of events leading to the 'natural ending' of the dominant. Does the reflex act potentiated or brought about as a result of summation at the dominant focus always lead to the natural end of the dominant, or does it not?

Let us return to one of the dominant models explored by Ukhomsky. Stimulation of cortical motor centres causes not limb movement, but enhancement of the CNS excitation focus being potentiated by the afferentation from the intestine. The summation results in the act of defaecation and the dominant discontinuation is thereby achieved. In the end, the impulsation flow from the intestine setting up the dominant focus in CNS comes to a halt. In this particular example, the summation at the appropriate centres launches genetically consolidated reflexes leading to the removal of the dominant receptive field. Distension of the intestinal muscles to a certain level produces its spastic contraction.

But supposing the reflex act due to summation does not stop the impulsation flow from the dominant receptive field. Let us take our 'polarization dominant' as an example of the case in point. The subthreshold excitation focus, produced in the sensomotor cortex and amplified to the threshold value by the excitation coming up via other afferentations, causes contraction of the limb. Since direct-current exposure continues unabated, the process is repeated, the reflex expression of the dominant follows a wavelike pattern and the dominant focus is clearly inhibited on a periodical basis, thus amounting, in effect, to a clinically observed model of tremor.

Protracted summation in the central apparatuses—when it fails to elicit a reflex act (dumb cortical areas) or when the reflex is elicited but not directed at the termination of the dominant (discontinuance of the impulsation flow from the receptive field of the dominant focus)—underlies the initiation and maintenance of a stagnant pathological focus and may form the basis for the pathogenesis of some diseases.

Thus, the reflex act evolving from summation in the dominant focus does not constitute per se the 'natural resolution' of the dominant as long as it does not arrest the impulsation inflow from the receptive field of the dominant focus (dashed arrow in Fig. 7.1).

Studies of numerous dominants in the animal's natural life favor the notion that the animal behaviour associated with the dominant focus that comes up in one or another CNS area has the primary goal of terminating the dominant. Accordingly, the animal's motivational behaviour directed to supplying a need leads to the termination of the dominant present.

In the case of feeding motivational behaviour of an animal this implies the cessation of the impulsation inflow from the receptive field of the stomach and circulatory system producing the dominant

state in the corresponding centres. Examining the importance of the dominant for animal behaviour one comes to see the rise of a dominant state in a particular motivational centre as a peculiar form of the SOS signal. The animal behaviour emergent on that basis is designed to terminate that state and establish in the CNS a sort of homeostasis. It would be useful to examine along these lines feeding, defence and sex-related animal behaviour.

Since the rise of endogenous dominant CNS foci provides, in the final analysis, an indicator of an upset state of balance with the environment, the realization of the behavioural act aiming to terminate the dominant is equivalent to the achievement of adaptational balance with the environment.

It is pertinent to ask: what underlies the goal-directed animal behaviour leading to the termination of the dominant?

In Ukhtomsky's work *The Dominant as the Operating Principle of Neural Centres* (1966) we may come upon exiting ideas about different dominant stages, which seem to bear directly on the understanding of the role of the dominant in behaviour. Derived as they were from a purely psychological observation of personages in Leo Tolstoy's novel *War and Peace* they deserve very close attention.

1. 'A sufficiently stable dominant, barely sketched in the organism under the influence of internal secretion, reflex influences and suchlike, pulls up to itself most diverse receptions as occasions for excitation.'

2. 'From the multitude of effective receptions the dominant fishes out the group of receptions that has very special biological appeal to it. This is the stage for the development of an adequate stimulus, as it is also the stage for the objective isolation of the given set of stimuli from the environment.'

3. 'Between the dominant (an internal state) and a given receptive content (a set of stimuli) there comes up a steady ("adequate") connexion whereby either of the agents (the internal state and the external image) will exclusively evoke and reinforce each other.' (*Ibid.*, p. 169.)

In Ukhtomsky's notebooks we find further extension of the third stage, except that he formulates it already as the law of backward relations: '... if reflex A, by way of irradiation, evokes another reflex B and then, in reverse, the reflex B evokes, by way of irradiation, the reflex A. Just as the flexion of the right hindpaw evokes secondarily the flexion of the left forepaw, so too, in reverse, the flexion reflex of the left forepaw evokes secondary flexion of the right hindlimb' (*Ibid.*, p. 246). The law of backward relations between the centres shows up clearly in having the defence dominant identified by another unconditioned reflex (Pavlygina and Malikova, 1978). When the defence state (the subthresh-

old limb stimulation) was identified repeatedly by the blinking reflex, further stimulation of the limb did cause its movement, but also blinking in the corresponding eye.

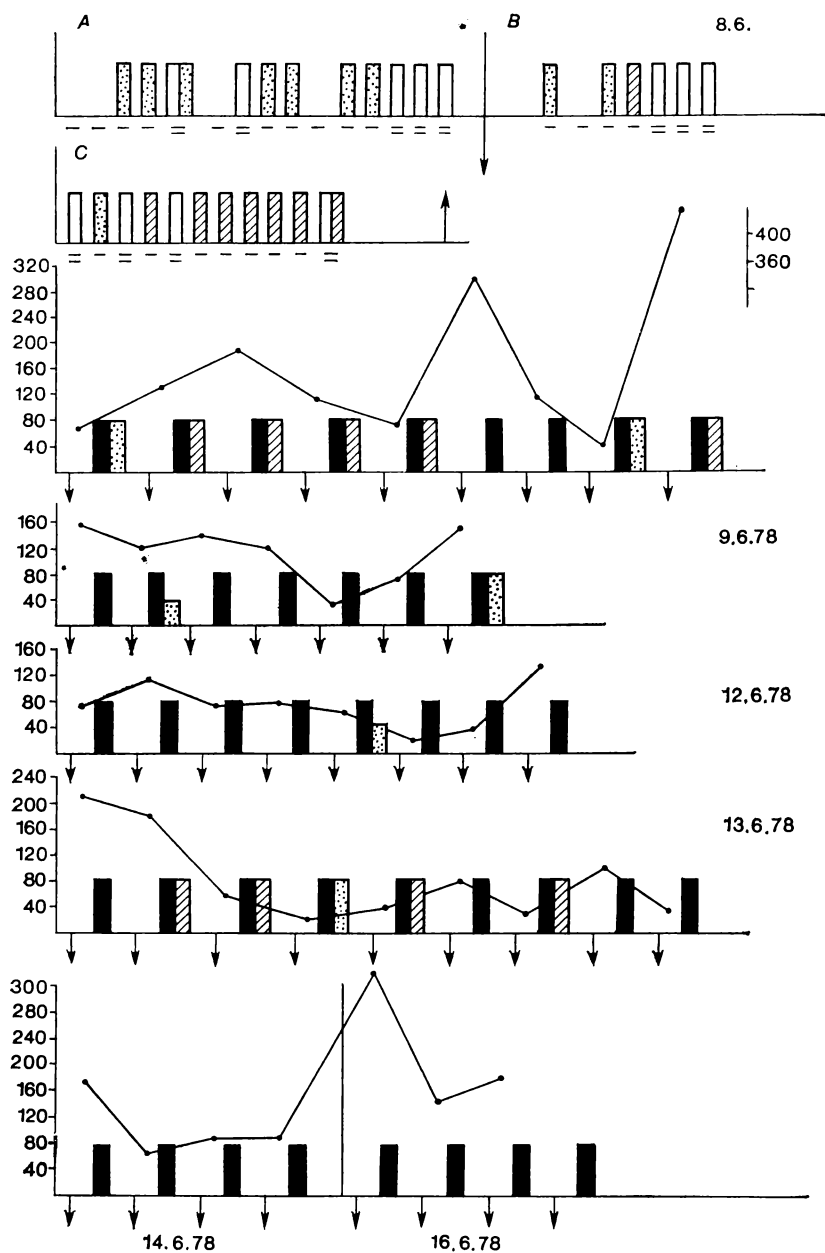
Here it is appropriate to recall Pavlov's conception of two-way conditioned connexion, confirmed experimentally by a number of his pupils and followers (Beritov, 1932; Kupalov, 1949, Varga and Pressman, 1963; Asratyan, 1966; Struchkov, 1973). That is, independent of each other, two Russian neurophysiological schools of thought, Pavlov's and Wedensky-Ukhtomsky's, came to recognize the law of backward relations both, in conditioned-reflex activity and under the dominant, a simple form of temporary connexion. This emphasizes likeness between the two phenomena and the universal nature of the mechanism of backward relations that encompasses all forms of temporary connexion.

Motivational animal behaviour will be discussed in the following section with some reference to the dominant stages identified by Ukhtomsky.

Analysis of motivational animal behaviour reveals that at the time a dominant appears the animal's behaviour is directed, in fact, to searching for an agent 'adequate' and 'specialized' for the dominant which has the capacity of solving, or terminating it (e.g. food terminates hunger). Primary verification of a stimulus or, more properly, a set of stimuli as to their 'adequacy' for the termination of the dominant proceeds by trial and error or else by the method of signal continuity, when young animals are trained by their parents. In all subsequent incidents of the dominant the animal's motivational behaviour will be guided by the pre-established temporary connexion to searching for an agent adequate for and capable of solving the dominant.

Ukhtomsky wrote on the inter-relations between the dominant and its adequate stimuli with special emphasis on the possible way of taking up a two-way connexion, alluded to in the previous discussion, when the appearance of the adequate agent may bring the revival of the appropriate dominant, refresh it in memory. Indeed, analytical treatment of animal behaviour has revealed that when temporary connexion comes to pass between the dominant and the adequate stimulus, the latter takes on the independent adaptive significance as a signal stimulus preparing the animal for a certain activity—given, of course, a dominant need. Realization of the backward connexion of a specialized dominant amounts, in effect, to a conditioned reflex.

We are aware of course, that this conception of the role of the dominant in animal's behaviour is schematic and leaves out many of the aspects in organization of behaviour, while saying nothing about conditioned behaviour. The primary goal of the present paper was to demonstrate that if motivational behaviour in



animals and human beings is to be properly interpreted from the neurophysiological standpoint, the dominant theory is a must.

While this is so, the dominant mechanism alone cannot and does not underly adaptive animal behaviour. The conditioned reflex and the dominant are links of a single process which vigorously participate in the realization of behaviour. Whether triggered by a signal stimulus (with a dominant need present) or a CNS-originating dominant focus, behaviour on the whole comprises the realization of a chain of temporary connexions on the basis of both these mechanisms—conditioned reflex as well as the dominant. The two mechanisms are but building blocks in the single edifice of behaviour.

The viewpoint on the dominant as a factor controlling behaviour guided our quest for experimental models that would bring us closer to an immediate understanding of the problem in question.

This was attempted on the starting assumption that protracted summation of excitations at the dominant focus with no possibility to achieve the realization of the reflex act that terminates the dominant produces a stagnant pathological focus. We took it from there to terminate the dominant, following the realization of a summation reflex to one of the agents used as the dominant 'potentiators'. For instance, the 'polarization dominant' was studied under the conditions when the reflex limb movement triggered by the summation led to the termination of the dominant (direct current is switched off).

The 'polarization dominant' was produced in rabbits by conventional means—setting the background of subthreshold direct current exposure (anode, 30  $\mu$ A current intensity, action through a thinned bone, electrode area 2 by 2 mm) in the representation area of the left forepaw in the cortex and using distant stimuli to trigger the desired limb movement (Fig. 7.2). The dominant focus was established also with a puff of air at the eye that has caused blinking, but also the movement of the left limb.

Once convinced that the dominant had been produced, we moved our grounds to the study of the dominant concluding stage. As an agent to terminate the dominant, the air-puff at the eye was used and the direct current was switched off, following the execution of summation to the air-puff at the eye.

Fig. 7.2. A graphic depiction of behavioural reactions of a rabbit in the study of the dominant concluding stage.

White columns are the blinking reflex to air-puff directed at the eye; columns with dots are the animal's general movement; shaded columns are isolated movement of the left forelimb; and black columns are voluntary blinking. One line under the abscissa identifies the moment of application of sound stimulus and two lines, the air-puff at the eye. The ordinate is time in sec. Dots joined together by a line show the time when voluntary blinking appears after direct-current switch-on. A—orientating reaction of an animal to applied stimuli before direct-current exposure; B—dominant summation stage; C—concluding stage; downward arrow is direct-current switch-on, and upward arrow is switch-off.

After a period of 30-40 minutes in the same experiment the dominant state was reproduced in the cortical centre of the left forelimb. Following direct current switch-on at different time intervals the rabbit has been found to blink his left eye—the very eye exposed to the air-puff during the summation stage. That is, the rabbit performed the reaction aiming to end the dominant state. The direct current was then switched off. Voluntary discontinuance of the dominant state by the rabbit was observed regularly in the former, and in all following experiments, as was to be expected (black columns in Fig. 7.2). The interval between the trials ranged from two to ten minutes. In some of the trials the voluntary blinking was accompanied by the movement of the left limb. The use of the distant stimuli in the time of direct current exposure could trigger the left limb movement in the early trials, whereas in the subsequent trials the dominant focus would not respond to the stimuli, as the dominant receptive field was narrowing.

Similar data have been obtained for all 21 rabbits. The only exception, was one rabbit in whom voluntary termination of the dominant state set in after a second application of the entire procedure with the dominant at the summation stage. For the other animals a single termination of the dominant upon achievement of the summation of the air-puff at the eye has been enough to obtain a steady temporary connexion between the dominant state in the cortical centre of the limb and the centre of the blinking reflex.

A study of the neocortex electrical activity at the dominant concluding stage has yielded the following findings (Fig. 7.3). Ordinarily, evoked potentials (EP) would be recordable at certain points in the sensomotor and frontal areas of the neocortex, in conjunction with the blinking caused by the air-puff at the eye (Fig. 7.3A). In voluntary blinking, leading to the termination of the dominant, a readjustment of the biopotentials similar in duration and form to EP occurs prior to the blinking, with EP almost totally lacking at the time of the reflex itself. The former potentials are recognized as readiness potentials (RP), because by continuous EEG recording the appearance of these potentials enables one to judge that voluntary blinking will not be long in following. The potentials differ by their amplitude and time of appearance (2-3 sec or just before the blinking) from the RP uncovered by a number of authors (Kornhüber and Deecke, 1964; Vaughan et al., 1968; Kotz, 1975; Kristeva et al., 1975) in the voluntary movement of the skeletal muscles. The latter have an amplitude of 10 to 15  $\mu$ V and precede the movement by a maximum of 1-1.5 sec. No RP studies in voluntary blinking have been made but, because the potentials recorded in our experiment indicate their 'pre-disposition' for the following blinking, they can be regarded as the RP of the voluntary



blinking reflex. A necessary note is in order about the difference, shown in Fig. 7.3, between RP localization at different neocortical areas and EP representation in blinking produced by the air-puff at the eye. RP have greater prominence in the frontal regions, yet another fact in support of the viewpoint held by some authors

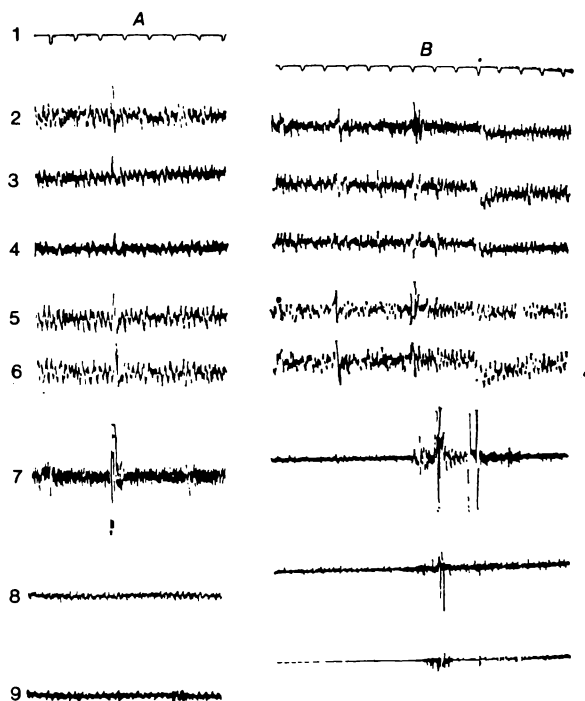


Fig. 7.3. Electrical activity of different neocortical areas in blinking reflex caused by air-puff at the eye (A) and in voluntary blinking (B).

(1)—seconds; EEG of frontal (2), sensomotor (3) and parietal (4) areas in the right hemisphere; EEG of frontal (5) and sensomotor (6) areas in the left hemisphere; electrical activity of eyelid muscles (7), right limb muscles (8) and left limb muscles (9).

(Luriya, 1966; Pribram, 1966; Anokhin, 1968; Andrianov and Molodkina, 1979) about the very special way that this particular region is implicated in the organization of goal-directed reactions.

To sum up the foregoing experimental evidence, one must conclude that the research findings identify the dominant concluding stage as the basis upon which a steady temporary connexion can be promptly installed between the centres in which the dominant focus has been produced and the centre to which the stimulus, leading to the termination of the dominant, is addressed. This temporary connexion is established in one experiment, following one or, at most,

two demonstrations to the animal of the way to terminate the dominant. In all subsequent experiments, as soon as the excitation focus reached a certain level, the rabbit performed a goal-directed reaction that terminated the dominant. That the goal-directed reaction takes place after the excitation focus, produced in the cortical centre of the limb movement, has attained a specific excitation level, is proved beyond doubt by the elicitation of blinking after a direct current exposure measuring in minutes, as a rule, and not immediately after the current switch-on.

A reminder should be given here that many investigators (Doty, 1961; Kandel and Benvenuto, 1973; Merzhanov and Serdyuchenko, 1975; Wagner et al., 1976; and others) who have actually used direct stimulation of various brain structures for the purpose of conditioning recognize the difficulty of the exercise and the need to employ a large number of stimulus pairings. Comparison of their data with ours prompts the conclusion that knowledge of what specific functional state is being initiated in the central apparatus is an essential input for the development of temporary connexion by direct CNS stimulation. The influence on the brain that sets up a dominant focus seems to be the very influence which is most adequate for the initiation of the temporary connexion. It is for good reason that the contribution of dominant-related occurrences to the elaboration of conditioned reflexes was acknowledged by a number of workers (Asratyan, 1941; Livanov and Polyakov, 1945; Pavlov, 1949; Skipin, 1951; Rusinov, 1957; Pavlygina, 1972).

The dominant-based temporary connexion exhibits the properties of forward and backward connexions. In our early experiments, the voluntary blinking accompanied by the left limb movement can be viewed as a demonstration of the backward connexion. When a focus with a certain level of excitation is produced as a result of direct-current exposure, activation of the blinking centres ensues. Voluntary blinking based on the principle of backward connexion leads to an increased excitation level in the cortical centres of the limb, driving it to perform the movement. In the subsequent experiments backward connexion is inhibited.

Investigation of the dominant at the concluding stage shows it to be the exact stage in the latter's development that may underlie goal-directed animal reactions as well as some forms of behaviour. When the dominant emerges from the concluding stage a temporary connexion is set up between the dominant focus and those centres whose activation brings the dominant to an end. The temporary connexion resulting from the dominant concluding stage is the one that forms the basis for goal-directed reactions in the animal.

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# 8

## The Reinforcement Function of Emotions

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The phenomenon of reinforcement is central to the conceptual system of the science of higher nervous activity. It is on reinforcement that any conditioned reflex depends for its elaboration, existence, extinction and distinctive characteristics. By reinforcement Pavlov understood the action of a biologically meaningful stimulus (food, harmful stimulus, etc.) imparting the significance of a signal to another stimulus biologically meaningless and paired with it. (Asratyan, 1971, p. 5.)

Numerous facts indicate that by pairing the so-called 'indifferent' stimulations one can elaborate a conditioned reflex, although the speed of the conditioned connexion establishment, its durability and further fate are decided by the animal's species characteristics, as well as the intensity, sensory modality and pairing sequence of the stimuli applied (Schoenfeld, 1978). Note that one should be too careful in referring to stimulus 'indifference'. What seems an indifferent stimulus to the experimenter may be ecologically important for the animal of the given species, not to mention that the exploratory need (curiosity) in many animals is so strong that it makes 'indifferent' events 'vitally important' (Berlyne, 1978).

As though sensing personally the formidable discrepancy and polysemy of the term 'reinforcement', I. P. Pavlov, in his final summarizing works (for example, the entry 'Conditioned Reflex' he wrote for the Large Soviet Encyclopaedia), had no use for the term and preferred to discuss the simultaneity of an indifferent and unconditioned stimulus. In a strict sense, one should call reinforcement the action of the second stimulus in their pairing sequency whereby the first stimulus begins to induce a reaction hitherto uncharacteristic for it. For all that, the biological significance of the second stimulus cannot be ignored, even in modelling conditioning by direct stimulation of cerebral structures in the study of cellular-synaptic mechanisms of conditioned connexions.

Markevich and Voronin elicited a conditioned pyramidal response combining a single bipolar electrical stimulation with a burst of three to five 100 Hz stimuli. Both electrode pairs were very closely spaced in a rat's sensomotor cortex in the representation area of

her forepaw. This combination was accompanied by stimulation of the point in the lateral hypothalamus which had triggered a self-stimulation reaction in preliminary experiments. Responses of the pyramidal tract were recorded in the medulla (see Diagram I in Fig. 8.1).

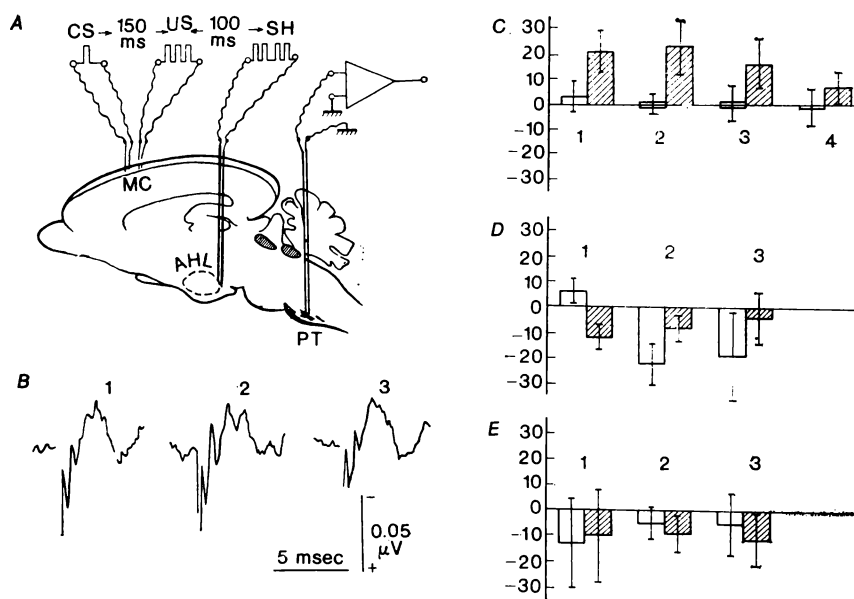


Fig. 8.1.

A—localization diagram of stimulation and lead electrodes in experiments with elaboration of conditioned reflex analog. Shown above are the intervals (msec) between the stimulations applied; B—examples of records of averaged pyramidal tract responses: 1—pre-pairings, 2—post-pairings, 3—post-extinction; C—summary changes of the direct and synaptic (hatched columns) components of the pyramidal response from data of seven experiments. The ordinate is percent changes relative to pre-pairing control, taken as 100 per cent: 1—during pairings; 2, 3, 4—consecutive series of extinctions; D—influence of hypothalamic stimulation before cortical stimuli (1); 2 and 3—after-effect; E—pairing of cortical stimulations without hypothalamic stimulation; 2 and 3—after-effect. For other explanations, see the text.

Fragments B and C in Fig. 8.1 demonstrate that the combination of all three stimuli enhances the synaptic components of the response but leaves the direct component relatively stable. None of these changes were observed in control experiments, neither by hypothalamic stimulation before the cortical stimuli (D), nor by packing of the cortical stimuli without additional stimulation of emotiogenic hypothalamic areas. Thus the participation of emotiogenic cerebral structures proves to be essential in eliciting a comparatively simple analog of the conditioned reflex.

The need to get the cerebral mechanisms of emotions involved in conditioning becomes particularly demonstrative in the case of instrumental conditioned reflexes, where the reinforcement depends on the subject's reaction to a conditioning signal. After a thorough analysis of the nature of instrumental conditioning Wyrwicka (1975) concluded that direct reinforcement is not the satisfaction of a particular need but obtaining desired (pleasant and emotionally positive) and eliminating undesired (unpleasant) stimuli. Depending on their intensity, the functional state of the organism and environmental characteristics, very diverse 'indifferent' stimuli may prove to be pleasant, such as light, acoustic, tactile, proprioceptive, olfactory ones, etc. On the other hand, animals are frequently known to spurn vitally necessary food ingredients when the food is not tasty. Hence the failure to elicit an instrumental conditioned reflex in rats by the introduction of food into the stomach through a cannula, i.e. avoiding the gustatory receptors. The same reflex, nevertheless, does develop following intragastric administration of morphine, known to induce promptly a positive emotional state in the animal. The same morphine, because of its bitter taste, ceases to be a reinforcer when it is delivered through the mouth (Cytawa and Trojiniar, 1976).

In another experimental series the authors elaborated an instrumental feeding conditioned reflex in rats and, once it was strong enough, replaced natural food by the intragastric supply of a food solution via a nasopharyngeal cannula. The lever-pressing reflex was thus extinguished as a result of the substitution, but persisted if a 0.05 per cent morphine solution was introduced intragastrically (Trojiniar and Cytawa, 1976).

These experimental findings seem to agree well with the data of Oniani (1975) who employed direct electrical stimulation of the limbic brain structures as reinforcement in conditioning. Pairing of the external stimulus with the stimulation of cerebral structures that had previously elicited feeding, drinking, aggression, rage and fear in a satiate cat achieved only a conditioned reaction of avoidance attended by fear after 5 to 50 pairings. It has not been able to initiate the conditioned reflexes of feeding and drinking. Neither can conditioned hunger be obtained in natural conditions: the environmental signals of the situation in which rats were starved evoked fear and the conditioned reaction of avoidance, but not feeding behaviour (Mowrer, 1960). A similar reaction was observed by Oniani in experiments with reinforcement of a conditioned stimulus by the stimulation of the 'aggression centres'.

After 110 pairings of sound and light with stimulation of the drinking hypothalamic region in goats, the conditioned signals did not elicit drinking behaviour, whereas the reinforcing stimulation provoked drinking immediately (Milner, 1973). In contrast, Fon-

berg did elaborate an instrumental conditioned reflex in dogs reinforcing it with the kind of stimulation inducing the satiate animal to feed. The author contended that in these trials the electric current activated the engrams of the signs of tasty food, but not the structures of hunger, which prodded the dogs to continue feeding despite the state of satiety (Fonberg, 1967).

Oniani argues that stimulation of the brain structures naturally activated by external factors (fear), and not by interoceptive impulses (hunger, thirst) can alone act as reinforcement. The possibility of avoidance conditioning with stimulation of the 'aggression centres' as reinforcement is explained by Oniani as resulting from the endogenous component—hormonal, as in wedding fights, or hunger—associated with the formation of natural states of aggression.

In our opinion these experimental findings are yet another proof of the decisive role of emotions in conditioning. Fear has pronounced aversion for an animal, which the latter seeks actively to minimize by way of the avoidance reaction. Stimulation of the drinking and feeding brain systems in animals experiencing neither hunger nor thirst provokes stereotyped acts of feeding and drinking but leaves the neural mechanisms of emotions uninvolved, thus excluding conditioned reflex development. With a given localization of the electrodes and parameters of the current, stimulation of the aggression centres generates an emotionally negative state which, as in the case of the emotion of fear, induces a minimizing reaction of avoidance.

Should aggressive behaviour in cats be accompanied by the engagement of emotionally positive structures, the latter's stimulation makes it possible to produce a conditioned reaction of self-stimulation, as shown by Valdman et al. (1976). The emotionally positive overtones of aggressive behaviour can also be detected in nature. Mice, for example, efficiently develop the lever-pressing instrumental conditioned reflex if this action is reinforced by the appearance in the cage of another mouse whom the 'actor' immediately attacks (Connor and Watson, 1977).

There is little point in discussing further the role of emotions in conditioning unless we are quite clear what *neurophysiological* reality we have in mind when using the psychological concept of 'emotion'?

In contrast with clinical-physiological investigations, where the physician maintains speech contact with the patient, the experimenting physiologist has nothing but the outward behavioural displays of an animal's emotions by which to judge these emotions. Here an obstacle arises, which Valdman repeatedly analyses in his writings. 'In estimating animal response reactions to electrical stimulation of the brain many experimenters make an overly sim-



plistic assessment of, and interpret in their own way, the essence of an animal's behaviour. Most proceed from the assumption that the emotion is a form of behaviour. An animal backing out and running away means the reaction of fear; if it is charging and attacking, this is the reaction of rage' (Valdman, 1972, p. 13).

Yet it has been repeatedly shown that both in natural conditions as well as in the electrical stimulation of the brain one is able to watch a quite goal-directed 'cold' attack, but without objective signs of rage; avoidance reaction of superb precision without symptoms of fear; ritual 'warnings' to the enemy (bristled hair, bared teeth and claws), without genuine anger.

Basing himself on the results of his systematic research, Valdman (1972) proposed to discriminate between: (1) emotional reactions—complexes of motor-vegetative manifestations characteristic of specific emotions that are not goal-directed ('pseudoaffects', according to older authors' terminology); (2) emotional behaviour—goal-directed behavioural acts with expressive signs of emotions; and (3) emotional states showing themselves only in the presence of appropriate test-objects in the environment (experimenter, another animal, signal of danger, etc.).

In an experiment on animals, a shift of the emotional state results from a weak (subthreshold) stimulation applied to those cerebral formations whose more intensive stimulation elicits emotional behaviour. In Valdman's opinion, 'it is these states, and not the varied manifestations that spring from stronger stimulation of these brain substrates, which can and must be qualified as analogs of emotions in animals' (*Ibid.*, p. 22-23).

Whereas Valdman considers it possible to take the 'emotional states' in animals as the analogs of human emotions, including those induced in patients by the stimulation of deep cerebral structures, Viliunas, a psychologist, is more pessimistic. 'A serious and, at first glance, insuperable barrier making the evolutionary principle somewhat difficult to apply to research on emotional occurrences arises from the fact that the emotional sphere of psychic reflection throughout biological evolution has remained absolutely inaccessible to direct investigation... Even our judgements about emotional experiences in higher animals represent, strictly speaking, only a supposition, an anthropomorphic projection based on the comparison of situations and behaviours' (Viliunas, 1976, p. 75).

We cannot agree with this assertion of Viliunas. As we see it, there are at least three possible ways for the experimenter to make an objective judgement on the emotional state of the test animal.

The first of these is to make sure of the presence, or lack of, vegetative shifts and characteristic changes in the bioelectrical activity of the brain, given that the physical load on the animal necessary to perform a motor act remains constant or declines during

the improvement of adaptive actions. If the animal, and in equal measure man also, executes the same motor skill, while the vegetative and electrophysiological shifts observed at the early stages of learning become increasingly weak, then there are grounds to postulate gradually diminishing emotional stress, since at present this phenomenon can be explained in no other way (Simonov, 1964; Preobrazhenskaya, 1969).

The second objective indicator of an animal's emotional state is the reaction of a second individual of the same species to the signals of emotional expression coming from the partner, the phenomenon of peculiar 'emotional resonance' (Valdman and Kozlovskaya, 1976; Simonov, 1976). Unlike the human observer, an animal is able to recognize subtle nuances of emotional expression in the partner that escape the experimenter.

But, the decisive criterion for the presence of an emotion in an animal, and not any other phenomenon of higher nervous activity, we firmly believe is to be found in the *attitude of the animal itself to the state of its brain*. The principle in question is the 'hedonistic principle of maximization-minimization'. The direct stimulation of the brain with an electric current is second to no other method in revealing either a *positive* emotional state, which the animal seeks to maximize, that is, to strengthen, prolong or relive, or a *negative* emotional state, which the animal, and in equal measure man, seeks to minimize, that is, to reduce, discontinue, or prevent. We emphasize that, the animal's emotion should be identified not by the character of the external factor (for food may cause a satiate subject's aversion and a destructive narcotic drug a pleasure), but by an active attitude to its own state manifested in behaviour. This particular behavioural criterion, rather than expression in the form of teeth baring, tail wagging, vocalization, etc., provides the experimenter with a decisive clue as to whether an emotional state occurs or not and whether it has a positive or negative coloration.

Moreover, the direct brain stimulation method is unable to answer another question: under the influence of what factors, with the help of what mechanisms, what cerebral formations participate in the activation of the emotiogenic structures in natural life, man's or animal's?

In the information theory of emotions (Simonov, 1964, 1981) emotion is defined as a reflection by the brain of the magnitude and quality of a need and the probability (possibility) of having it satisfied at a given moment. The satisfaction probability is prognostically evaluated by the brain basing itself on the born or previously acquired experience. Other necessary inputs include the proficiency of skills, the energy resources of the body and the necessary and sufficient time to carry out adaptive actions. This kind

of evaluation results in the excitation of a system of specialized cerebral structures driving the subject to alter his behaviour towards minimization (reduction, discontinuance or prevention) or maximization (strengthening, prolongation or repetition) of such a state.

The information theory of emotions originated from I. P. Pavlov's works on the systematic principle in the activity of the brain cortex and his idea about the signs of emotional stress said to appear as a dynamic stereotype is formed or disturbed. I. P. Pavlov presented his views on this on August 24th 1932 at the 10th International Congress of Psychologists in Copenhagen and, a week later, at the 14th International Congress of Physiologists in Rome on September 2nd 1932. In more recent years Hodge (1935), Hebb (1946) and Magda Arnold (1960) aired some concepts not at all dissimilar with this Pavlovian perception of the decisive role of the dichotomy between the previously established internal stereotype and the really existing external stereotype in the genesis of emotions. The mismatch between the acceptor of the results of action and feedback afferentation is central to P. K. Anokhin's biological theory of emotions (1964). What matters most for the information theory of emotions is the brain prognosis not only of the content of a goal, but also of the probability of its achievement, and hence the name of the conception proposed by this author. Carl Pribram too came to embrace similar views (Pribram, 1967).

The theory is as valid for complex behavioural acts as it is also for the origin of any emotional state, including the emotional pitch of sensations. For example, a positive emotion in feeding arises after the integration of the hunger excitation (need) with the afferentation from the mouth cavity, indicative of the growing satisfaction probability for the given need. In another state of need the same afferentation generates a sense of indifference or the negative emotion of aversion.

Physiologists spent many years trying to locate the cerebral formation playing the decisive role in the genesis of emotional states, the likely candidates including the hypothalamus, thalamus, hippocampus, reticular formation, etc. The trend left its mark on the names of the respective theories, known as 'thalamic', 'hypothalamic-limbic', and 'activational'. The latest modification of such an approach to the emotion localization problem is found in McLean's ideas (McLean, 1970). To him, the hypothalamus is the representation region of the stereotyped forms of behaviour which, as a rule, are accompanied by emotions (reactions of defence, attack, search, and procurement), whereas specific motivations are associated with the overlying brain regions. It is thus said that the needs of self-preservation (hunger, defence, etc.) reside in the amygdala; reproduction and sex in the septum; zoo-social, group

and gregarious motivations in the cingular and prefrontal cortex; and the neocortex of higher vertebrates is the accumulation site of their individual experiences.

Nevertheless, experiments with direct electrical stimulation of different cerebral formations, and with their destruction as well, argue against the conception of a particular structure as the local 'centre' for the emotions of fear, rage, pleasure, etc. Even complete surgical removal of the hypothalamus in cats does not result in the loss of defence and feeding responses with their telltale emotional shading (Ellison and Flynn, 1968). Summing up the existing situation Valdman remarked, 'In principle, attempts at topographic representation in the brain of "emotions", as of other psychic functions, are an echo of localizationism... The question concerning "the substrate of emotions" can be presently answered with certainty only as regards the topography of the integrative centres (regions) of emotionally expressive manifestations' (Valdman, 1972, pp. 14-15). This notion is consonant with that of Smirnov '... it is hard to name the brain structures responsible exclusively for emotions... I agree therefore with Valdman that neurophysiological investigation of emotions and emotional behaviour must not be directed at searching for the structural elements of emotions; rather it should be based on the systematic principle' (Smirnov, 1976, p. 166).

Recognizing as we do that the present disappointment with the results of the search for 'point'-localized emotigenic structures is well-grounded, we still believe that there can be no going back to the former diffuse idea of emotions as a function of 'the brain as a whole' or the result of 'cortical-subcortical interrelations'. Despite the extreme complexity of the problem the experimental neurophysiology of emotions cannot give up the fundamental 'assign-dynamics-to-structure' principle inherited from I. P. Pavlov.

It is next to impossible nowadays to find a researcher who would still conceive of the neural 'centres' of emotions as a limited nerve tissue site. Anyone who attempts to examine the organization of the cerebral substrate of emotions invariably is bound to refer to a system or a broadly ramified constellation of neural formations represented on different cerebral levels in higher animals or humans. The idea of the dominant focus having particular relevance to the neurophysiology of emotions is as a 'functional organ', or a system—the concept we associate with Ukhtomsky. 'Dominant focus', says V. S. Rusinov (1967, p. 200), 'is Ukhtomsky's "constellation" formed as a system during current activity of the organism—at all levels of the central nervous system in its different parts, but with a primary focus in one part and with a variable role for functions of individual components of the system'. Ukhtomsky emphasized the achievement of a certain result as the very

factor which develops the functional organ into an integral whole. 'With the name of 'organ' we habitually associate the idea of a morphologically established, and statically permanent formation. This is not necessarily so. For an organ may be any temporary combination of forces, *capable of certain achievement*' (Ukhtomsky, 1950, p. 279. *Italics mine*—P. S.).

But, no matter how much we talk about the 'systematic principle' and the 'modulating' and 'regulating' effect of cerebral formations upon one another, it will make little sense until specific experimental evidence has provided a key to the specific role of any particular link of the system in the genesis of a given emotional state and the specific contribution of this link in the organization of an integral emotional reaction.

According to the information theory of emotion, needs, motivations and emotions not only represent independent phenomena of higher nervous (psychic) activity not to be identified with one another, but must of necessity possess a morpho-physiological substrate of their own. Mikhailova and Sarkisova have carried out experiments in our laboratory that we are sure set out in high relief the consecutive pattern of involvement in the organization of behaviour of the cerebral mechanisms for needs, motivations and emotions. The method they employed of gradually stepping-up the stimulating current intensity has long been used by Valdman, Kozlovskaya, Houston and other workers.

Twenty-two male albino rats had monopolar steel electrodes 60  $\mu\text{m}$  in tip diameter implanted into their lateral preoptical region and lateral hypothalamus (their König and Klippel Atlas coordinates A-7; L-1.8; H-3.5; A-3.0-3.5; L-1.5; H-3.5). During the stimulations the chamber contained a pedal for self-stimulation and the goal objects to identify specific motivations, namely, feeding (sunflower seeds or oats strewn uniformly on the floor), drinking (a bowl of water), gnawing (a piece of chalk or wood), and sexual (a female). The stimulation was by means of rhythmical current (rectangular monophasic pulses 100 Hz in frequency, 0.1 msec in length, and from 0 to 1.0 mA in intensity) or direct current 0 to 70  $\mu\text{A}$  in intensity. Consummatory responses (feeding, drinking, gnawing) were registered by recording the chewing muscles myogram. The latent period and the probability of the reactions, i.e. the ratio of the quantity of the stimulations eliciting these responses to their total number were estimated. The reinforcing effect (emotionally positive) of the current was estimated according to the frequency of self-stimulation. Prior to the experiment the rats had been given unrestrained access to food and water.

The stimulation was applied exclusively to the areas able to yield a self-stimulation reaction if acted-upon by the current of adequate intensity. It was found that by polarization of the areas with

gradually increasing direct current or stimulation with rhythmical current of increasing intensity the behavioural reactions thus produced always follow the same sequence. Weak stimulation elicits

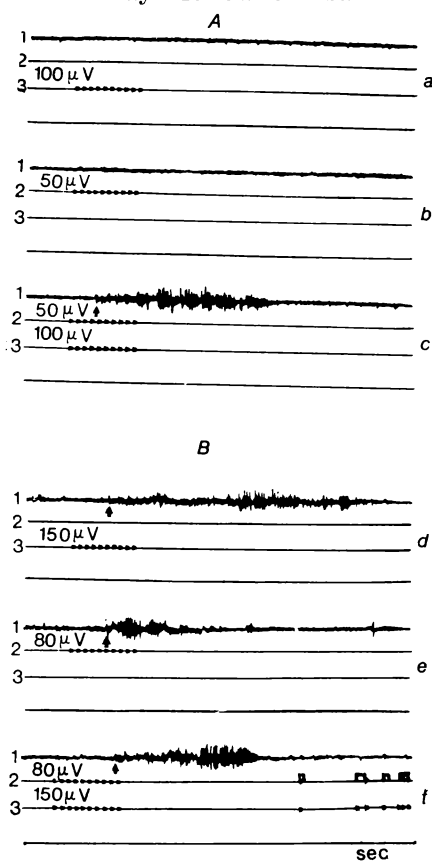


Fig. 8.2. Effects of simultaneous stimulation of two hypothalamic points with a rhythmical current of 'searching' (A) and 'motivating' (B) intensity.

1—myogram of chewing muscles; 2 and 3—stimulation of the first and second point. The deflection of line 2 in segment 'f' identifies self-stimulation

point. White (1973) reported the cessation of natural feeding behaviour by the stimulation of the amygdala strong enough to evoke self-stimulation.

In Mikhailova and Sarkisova's experiments, direct current application clearly had a methodological advantage over stimulation by rhythmical current. The rhythmical current stimulation of two

generalized searching activity without recourse to the goal objects present in the chamber, i.e. food, drink and an individual of the other sex. Only after the stimulation intensity had been augmented did those external stimuli become effective in getting the animal to start feeding, sometimes drinking, gnawing, and so forth. With further enhancement of the rhythmical or direct current, the self-stimulation response ensues.

When two different points in the hypothalamus were stimulated, the observed sequence has been similar. Whereas two stimulations of the 'searching intensity' produced consummatory responses, usually feeding, less often drinking, gnawing, etc., two stimulations of the 'motivating intensity' have been able to trigger a self-stimulation response (Fig. 8.2).

The action on one of the points, sufficient to produce self-stimulation, inhibited the motivated behaviour initiated by the stimulation of the second

points makes the self-stimulation responses stronger (more frequent). Weak cathode polarization of one point inhibits the self-stimulation of a second focus while increasing the intensity of the direct current enhances the self-stimulation. Note that the inhibitory action was exerted by the direct current intensity which causes goal-directed motivated behaviour if applied in isolation.

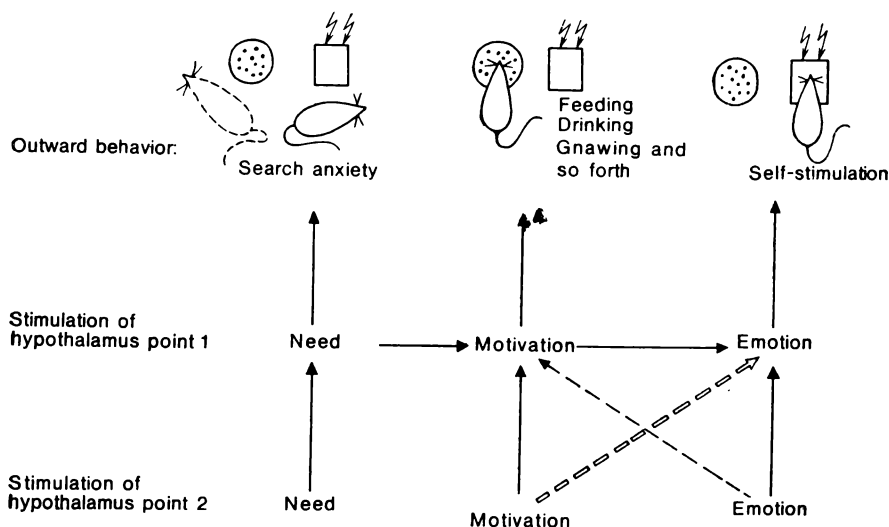


Fig. 8.3. Diagram illustrating the effects of simultaneous stimulation of two hypothalamic points. Solid arrows indicate summing effects. Broken arrows show the inhibitory influence of stimulation with a rhythmic and direct current (a thin arrow), and a direct current alone (a double arrow).

The observed transformation of effects is hard to explain in terms of non-specific additional activation of 'the motivational reinforcing' structures. This was because the stimulation of the emotionally negative (avoidance-inducing) regions of the midbrain reticular formation had an inhibitory influence upon self-stimulation (Mikhailova, 1975); but the stimulation of the emotionally neutral areas exerted no influence at all on self-stimulation of the hypothalamus. Thus the excitation of the emotionally positive structures of the reticular formation, able to elicit at least a weak self-stimulation, is the only one that summates with 'searching', 'motivating' and 'reinforcing' excitation of the hypothalamic structures.

We consider that model experiments of the kind described above

reconstruct the course of events characteristic of the organization of natural behaviour (Fig. 8.3). Weak electrical stimulation activates the system of brain structures representing the substrate of a need. The need actualization process, not yet transformed into motivation, has the outward appearance of a generalized searching anxiety. Only by increasing the excitation while stepping up the intensity of the direct or rhythmical current can those structures, which store the engram of the external objects capable of satisfying the need, be activated. As a result, the external stimuli become effective and the motivated animal starts feeding, drinking, gnawing, etc. However, a further increase of the current is necessary to activate the emotionally positive reinforcement structures and get the animal to move on to cerebral self-stimulation in the absence of natural means of satisfying its specific need.

Clearly, our concept is not that the structures of the need, motivation, and emotion are linearly disposed, as it were, in neighbouring parts of the brain tissue, to be captured in succession, one after another, by an electric current of increasing intensity. Rather, the system of structures necessary and sufficient for need actualization is more simple and includes fewer elements than the system ensuring goal-directed behaviour of the animal. The complex of the morphophysiological organization of behaviour (need+motivation+emotion) to be complete requires the additional involvement of the neural apparatus of emotion.

To understand the consequences of stimulating two hypothalamic points with electric current of different intensity it is worth bearing in mind the findings of the research on the mechanisms of natural feeding behaviour conducted by Shuleikina, Olds and others.

Shuleikina (1974) showed that hunger excitation (actualization of the need for food) arises first in the reticular nuclei of the pons and medulla and extends later to the central grey matter of the midbrain, non-specific nuclei of the thalamus, and the dorsal hippocampus. In order to transform the actualized feeding need into a goal-directed search for food, further involvement of the structures of the neocortex, amygdala and 'positive elements' (Shuleikina's term) of the medial hypothalamus are required.

Let us note that the hypothalamic structures begin their active functioning at the stage of the food-getting search initiated by the hunger excitation. In the lateral hypothalamus of hungry monkeys there are neurons which respond with modified activity to the sight and smell of food, and the conditioning signals of the coming feeding (Olds, 1977). There, too, in the lateral hypothalamus, neurons may be found that are likewise activated by other needs, say, thirst or morphine abstinence in rats.

An animal comes into contact with food and starts the feeding



act, realized by the synchronizing system of the lower region of the brain trunk, thalamus, visual cortex and lateral hypothalamus. Neural impulses arriving from the mouth cavity and then from the stomach signal the impending satisfaction of hunger. It has long been known that this kind of afferentation stops the feeding act long before true 'tissue' saturation. The process was vividly described by I. P. Pavlov in 1910-1911: 'A small amount of food entering the stomach temporarily ceases or reduces the action of the food centre... The state of affairs would be worse if the excitability of the food centre fell only when the satisfaction of the organism's need for liquid and solid nutrients is complete, for overeating, or excessive filling of the stomach with food, would then be the constant aftermath of such a condition' (Pavlov, 1973, p. 108).

At the very beginning of feeding the arrival of food continues to activate 'positive' neurons in the medial hypothalamus; but in the course of satiety 'negative' neurons are activated that have an inhibitory influence on the neurons in the lateral hypothalamus previously hunger-excited, and food intake comes to a halt.

We agree with Shuleikina in the contention that the conclusion about localizing the 'hunger centre' in the lateral and the 'satiety centre' in the medial hypothalamus oversimplifies reality. We are inclined to identify the structures of the lateral hypothalamus predominantly with the processes of feeding motivation in all of its stages, from the hunger excitation bringing lateral hypothalamic neurons to respond to the conditioning signals, the sight and smell of food up to the state of satiety. As for the 'positive' and 'negative' elements of the medial hypothalamus, changes of their activity give grounds to class them with the neural mechanisms of *emotions*—positive, in the period of imminent feeding and at the beginning of feeding, and negative, progressively activated as food is ingested.

Let us return to the analysis of experiments with electrical stimulation of the hypothalamus. The weak current stimulation presumably imitates the hunger excitation which in nature arrives into the hypothalamus from the reticular nuclei of the pons or medulla. The excitation must be augmented by stepping up the electric current intensity or by stimulation of a second 'food' (and not each or any) point to activate the engrams of the feeding objects and elicit the act of feeding. During the feeding process the neural elements generating an emotionally positive state are excited, but again this excitation falls short of effecting a transition to artificial electrical stimulation of the emotionally positive structures. Only further amplification of the current or the summation of two 'motivating' excitations can replace feeding by self-stimulation. It is worth re-emphasizing that the phenomenon of artificial reinforcement is by no means a consequence of increased motivational exci-

tation. Not the excitations of motivational structures are summated, but those of the emotionally positive elements, because the shift from feeding to self-stimulation takes place only through the stimulation of the points each of which is capable of eliciting a self-stimulation reaction, given a sufficient current intensity.

In the rat the shift to self-stimulation gradually halts feeding behaviour (the corresponding inhibitory influence is illustrated in

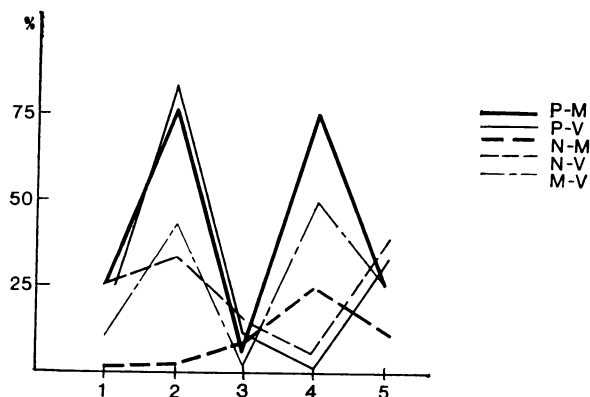


Fig. 8.4. Percent incidence of statistically significant changes in coherence of electrical activity of brain structures at different phases of self-stimulation in rats.

1—quiet state; 2—before lever-pressing; 3—on the lever; 4—before moving away from the lever; 5—immediately after moving away. P—emotionally positive point in hypothalamus; N—emotionally negative point; M—motor cortex; V—visual cortex

Fig. 8.3 by a thin broken line). This effect is yet another indication that the direct reinforcer of the instrumental reflexes is not the satisfaction of a need but the maximization of a positive emotional state or the minimization of a negative one. The inhibitory action of the stimulation of the motivational structures upon the self-stimulation response was only possible to be identified by direct current exposure (shown in Fig. 8.3 by a double broken line). This inhibitory influence reveals, as we see it, that nothing other but the activation of the structures of positive emotions is the basis of self-stimulation. Depending on the degree of the hunger excitation present, the same afferentation about the coming satiety (or its imitation by electrical stimulation of the proper brain structures) may eventually prove either sufficient or insufficient for the activation of positive emotions. In the latter case, the increasing motivation leads to the excitation of emotionally negative elements and inhibits the self-stimulation reaction.

An analysis of the spatial organization of neural processes based

on the methodology developed by Livanov and his associates (Livanov, 1972) has provided very productive insights into the physiological mechanisms for the participation of emotions in the organization of behaviour. Polarization of the 'Olds centres' in rats by the Rusinov method offered a unique opportunity of recording the electric activity of the polarized structures and comparing the activity (computation of coherence functions) with the electrograms of other cerebral formations. Our experiments conducted with Pavlygina, Trush and Mikhailova (1977) (Fig. 8.4) have established, that shortly before a rat pressed the lever and immediately before it moved away from it, there was an increase in the percentage of incidents with significantly greater coherence of the rhythms dominant in the frequency spectrum of the electrograms of the motor cortex, the emotionally positive point in the hypothalamus (before pressing) and the emotionally negative point in the operculum (before moving away). The experiments highlighted the function of emotions as a control regulating the duration of contact with the source of artificial reinforcement.

Recall that, according to Livanov (1972, p. 88), spatial synchronization of the bioelectrical activity of different brain formations demonstrated '... not ways of the reflex connexion but those of the influences which make the transmission of excitation possible in the brain cortex'. The experiments have shown that, depending on one or another stage in the organization of behaviour, the excitation of emotionally positive and emotionally negative structures may enter the neural elements of the motor system, transforming itself into the reaction of approach or avoidance.

A schematic representation of the role of emotions in conditioning is attempted in Fig. 8.5. Since its very inception, the conditioning theory presumed the convergence of two excitations, the one from the conditioning stimulus and the other from the unconditioned stimulus, e.g. the afferentation from the mouth cavity with the arrival of food into the mouth (Fig. 8.5, *II*). At the same time the significance of the 'existing functional state', that is, the feeding excitability which we see today as resulting from the excitation of the brain structures activated by the emergence of an appropriate need, such as the state of hunger, was elucidated (Fig. 8.5, *II*). However, neither the afferentation from the mouth cavity, nor the hunger excitation are able to play by themselves the role of a reinforcement and provide instrumental conditioning. Only integration of the hunger excitation and that from the factor able to satisfy a given need, i.e. the mechanism generating a positive emotion, can ensure conditioning. With any other correlation of the converging excitations, such as, for example, by food arriving into the mouth of an overfed animal, the activation of the negative emotion mechanisms leads to the defence reaction of avoidance (Fig. 8.5, *III*).

We would like to conclude by emphasizing the following point. While I. P. Pavlov's writings make only casual references to emotions, senses and drives and contain unattached statements to that effect, which nonetheless turned out to be extremely promising with a potential for future experimental research, the neurophysiology of motivations and emotions has now developed as an essential discipline in the science of the higher nervous (psychic) activity of

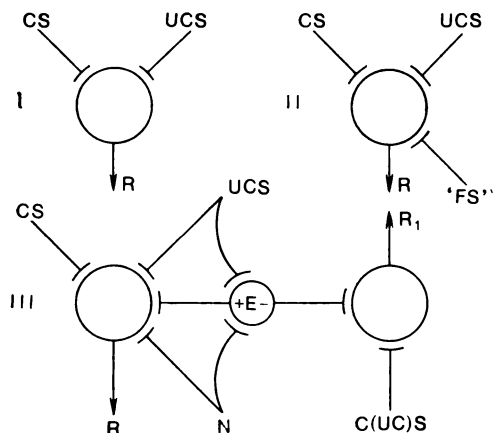


Fig. 8.5. Two- (I), three- (II) and four-factor (III) diagrams of excitations meeting at the point of convergence in conditioning.

CS—conditional stimulus; UCS—unconditional stimulus; R—response; FS—functional state; N—need; E—emotion

man and animals. We need only say that without taking proper account of the neurophysiological mechanisms of emotions we can hardly expect to solve the key problem in the physiology of higher nervous activity—the locking mechanism of conditioned reflex.

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# 9

## Two-Way Conditioned Connexions and Their Role in Motivation Mechanisms

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### 9.1. TWO-WAY CONNEXION AS A GENERAL NEUROPHYSIOLOGICAL PRINCIPLE

The achievements of classical and modern neurophysiology give sufficient grounds to see reflex as a universal phenomenon in the activity of the whole central nervous system—from the roots to the top. Over the developmental history of the animal kingdom reflex reactions have attained vast diversity in certain of their attributes, such as functional specificity, biological significance, degree of complexity, level of perfection, origin and a few others. And yet they share some substantive common features of principle. This is one reason why the findings of the research of elementary reflex forms provide useful insights into our knowledge of the essence of their more complex and higher forms. For example, we can point out the stimulating influence of inborn reflexes of Bahnung, convergence and common path, inductive and power correlations, established from the study of inborn reflexes, on the identification of the same regular principles in conditioned reflexes later on.

As early as 1912 Pavlov (1973) introduced the idea that at times the results of investigations into complex and high-level reflexes, which conditioned reflexes are, may be useful for research on unconditioned reflexes, known to be inferior to them in rank and functional architecture. He emphasized one essential research advantage of conditioned over unconditioned reflexes—the advantage of providing the experimenter with the chance ‘to see the very process of formation of this reflected act’, to follow its initiation, dynamics and regular patterns, and also the formation of its properties. The unconditioned reflex, conversely, presents itself to the experimenter ready-made. The validity of this idea of Pavlov’s was subsequently confirmed by the data of a number of researchers to the effect that in the process of ontogenetic evolution unconditioned reflexes went through some phases of generalization (‘mass action’), specialization and localization, i.e. the phases previously established for reflex elaboration and formation.

Of all other possible examples illustrating the validity of this profound Pavlovian concept, we shall limit ourselves to just one, namely, the phenomenon of two-way connexion in reflex activity. Investigation of this important phenomenon in the overall context of conditioned reflex also shows a substantive advantage over its investigation of unconditioned reflexes—the advantage of making the experimenter not only a witness to the origination and formation of two-way conditioned connexion but one who is capable of active control over the processes to suit his formulated goals and elicit conditioned reflexes of the types bringing into sharp focus two-way conditioned connexions so as to render them convenient for experimental analysis and investigation.

The idea of two-way conditioned connexion was borrowed by physiologists from psychologists who discovered, in particular, the two-way associative connexion between the meaningless syllables that arises in combining them in man (Ebbinghaus, 1885). In the new scientific field the idea was initially applied to the interpretation of facts then available and in dissimilar ways by different scholars.

Pavlov (1973) considered that two-way connexion was locked between the cortical points of the signal and reinforcing stimuli and that a forward connexion (from a first to a second point) and backward connexion (from the latter to the former) were endowed with similar functional properties. He believed, in addition, that the activation of the backward conditioned connexion was basic to the accomplishment of instrumental reflex and voluntary movement.

Beritov (1960), conversely, was of the opinion that these forward (or progressive, to use his term) and backward conditioned connexions carried out diametrically opposite functions. To him, the activation of the first connexion was followed by the performance of the appropriate conditioned reflex. The activation of the second connexion due to the emission of reinforcement led to the blockade of the former connexion and the reflex effected through its medium. It also led to the development of the phenomena known as extinction, differentiation and delayed inhibition of conditioned reflexes. Pavlov regarded them as a manifestation of internal inhibition (Beritov challenged then the capacity of the neocortex to develop inhibition). What Pavlov's and Beritov's ideas of two-ways conditioned connexion had in common was that both these concepts in the words of Gormezano and Tait (1976) were equally speculative and of a verbal character.

Later the pupils of both Pavlov (Skipin, 1947; Kupalov, 1949; Fedorov, 1955; Pankratov, 1955 and others) and Beritov (Bregadze, 1956; Javrishvili, 1956) elaborated a number of new instru-

mental and classical conditioned reflex varieties, thus expanding by far the scope of those original facts that had previously led both their teachers to assume the formation of two-way conditioned connexion. As to the validity of the assumption itself, it still remained to be proved. Meanwhile the necessity for a clear-cut solution to the issue, based on adequate experimental facts, could not be more obvious. It suffices to mention that, though Pavlov, in deriving his idea on that matter, drew for his analysis upon facts about instrumental conditioned reflexes studied most systematically and consistently by Konorsky (1967) and his colleagues and though Pavlov's concept of two-way conditioned connexion as a major characteristic trait in the functional architecture of the above conditioned-reflex variety appeals by its logic and elegance, nevertheless Konorsky himself did not share these views and interpreted the mechanism for the reflexes in a very different manner.

Special and systematic experimental research was needed to answer definitely and precisely the question of whether two-way conditioned connexion really existed and, if the answer was affirmative, to identify and examine carefully the latter's functional peculiarities, interaction, degree of expression in the various conditioned-reflex modifications, role in the activity of the cerebral cortex and so on. Such research is carried out in two main laboratory groups: Dostalek (1964) with associates in Czechoslovakia, and Asratyan with coworkers in the USSR.

In methodological terms our investigations in that area are essentially different from those above. Their common guidelines are as follows. For the purpose of conditioning, we variously combine, as a rule, the stimuli eliciting own specific inborn reflexes in their natural effector manifestation that are clearly definable, easily graphically recordable and biologically meaningful. Specifically, we manipulate different combinations of food, electrical stimulation of paws, orbicular eye muscle, different areas of the neocortex and subcortical formations, oral introduction of milk or acid solution through special cannulas, passive paw flexion, and local skin cooling. This enables us to follow closely the variational dynamics of the own reflexes of the stimuli being combined for the purpose of reflex elaboration and specialization and then, by testing stimulation of each of the paired stimuli, to define strictly objectively whether the conditioned connexion brought about between them is one- or two-way. For the same reasons we also record graphically the specific inborn reflexes of the so-called indifferent stimuli—visual, acoustic, tactile, etc.—when pairing them with one another or each of them with one of the previously mentioned biologically meaningful stimuli.



Over the last decade, in parallel with the graphic recording of the studied reflexes in their effector manifestation we record also electrical activity—EEG, evoked potentials, neuronal discharges and other similar occurrences at the cortical projection points of the paired stimuli before and during the formation of a conditioned connexion between them.

Experiments carried out mostly on dogs and cats have led the following facts being established among others. The combined use of

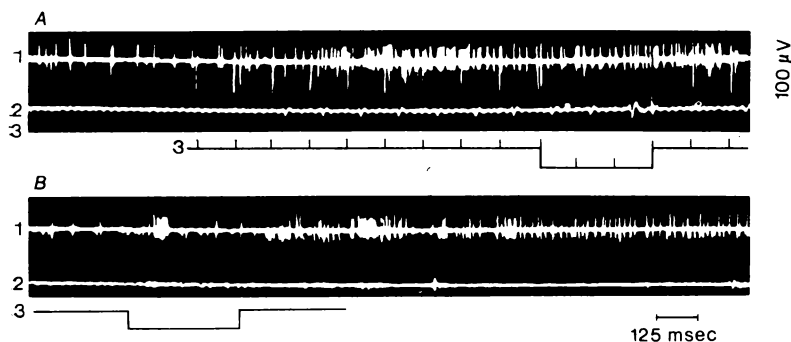


Fig. 9. 1. Neuronal activity of visual cortex (*I*) after elaboration of conditioned instrumental food procuring reflexes to a visual stimulus.

*A*—during application of the conditioning stimulus; *B*—during food presentation; 2—EMG of the “instrumental” paw; 3—the application of conditioning and reinforcing stimuli (after Merzhanova and Serdyuchenko, 1977).

any of the enumerated stimuli usually results in conditioned reflexes with a two-way connexion so that the separate action by either of the paired stimuli elicits not only its characteristic inborn reflex but also a reflex induced by its partner stimulus. This applies to the elaboration of both classical and instrumental reflexes. This fundamental fact was established not only through registration of the natural effector manifestation for the appropriate reflexes, but also by recording of summary or neuronal electrical activity at the cortical points of the paired stimuli prior to and during the elaboration of a specialized and stable conditioned reflex (Fig. 9.1).

In this context recent experimental findings by our colleagues are interesting. In cats they elaborated alimentary conditioned reflex with milk reinforcement to low-frequency electrical stimulation of the lateral geniculate body and kept an on-going record of neuronal activity in the visual and sensory motor cortical regions. Sta-

tistical analysis of the activity of the neuron groups in either area on a Plurimat S-100 computer by plotting cross-correlograms between the two groups showed that, following conditioning, a new form of interaction between the visual and sensory motor cortical neuron groups becomes established as a result of the formation of two-way conditioned connexions (Fig. 9.2). When the stimuli application in pairs follows a standard sequence and, with time, a conditioned reflex becomes increasingly strong, the inborn reflex of the first stimulus in order of application becomes attenuated, sometimes to the point of complete disappearance, this reflex may still be elicited by the action of the second stimulus but already as a conditioned reflex. When, on the contrary, the conditioned reflex to one of the paired stimuli is extinguished by the well-known

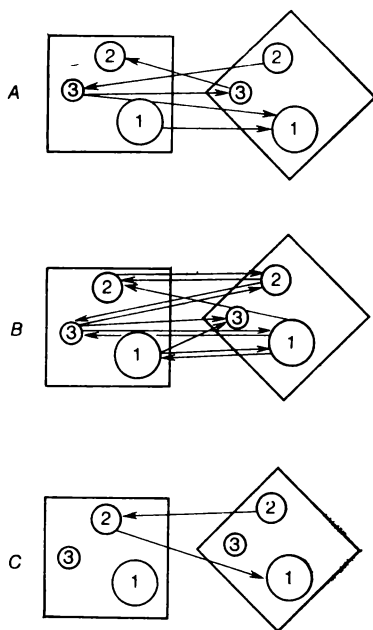


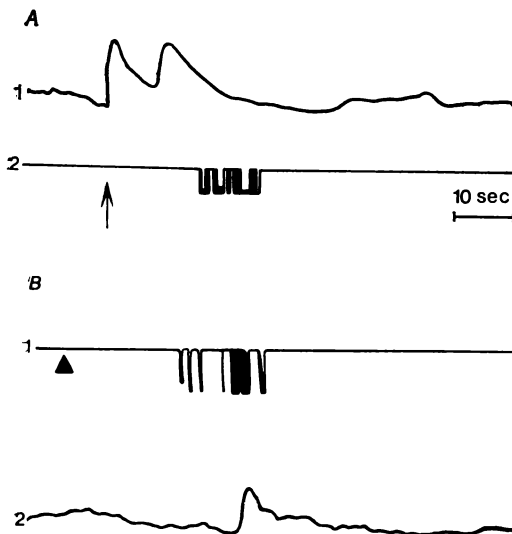
Fig. 9.2. A picture of connexions between cortical neurons of the visual (to the left) and sensory motor (to the right) regions.

A—before and C—after reflex conditioning; B—after extinction of the conditioned reflexes (after Merzhanova et al., 1981)

method, the conditioned reflex to the second stimulus may nonetheless persist (Fig. 9.3). As well as our other experimental evidence, these facts suggest clearly that two stimuli in combination generate between them not one conditioned connexion with a capacity to transmit the excitation alternately in one or another direction but two independent connexions that conduct the excitation in opposite directions. They are (1) forward connexion, from the cortical point of the first stimulus to the cortical point of the second stimulus; and (2) backward connexion, from the second point to the first. Essentially, the acquisition of two distinctly different conditioned reflexes takes place.

Additional evidence that forward and backward connexions exist independently of each other is provid-

ed by the way they originate not in strict concurrence and commonly differ in their stability and strength. As a rule, forward conditioned connexions are formed earlier as backward connexions and are more durably and regularly manifested. However, both these conditioned connexions are as dependent for stability as they are for the intensity of the reflexes actuated through their medium upon a host of other circumstances: biological significance and intensity of paired stimuli; functional state of the recipient cerebral structures and general state of the organism; and the type and specific features of the reflexes being conditioned.



**Fig. 9.3.** Defensive-alimentary conditioned reflexes in molluscs. **A**—tactile stimulus (↑) elicits conditioned pneumastom closure (1) and unconditional biting response (2); **B**—food (▲) elicits unconditional biting response and conditioned pneumastom closure (2) (after Maksimova)

Yet the independence of the connexions and the conditioned reflexes they mediate is relative, as they are intimately related and interactive. Very deep extinction of the conditioned reflex to one of the stimuli, for example, entails gradual attenuation and blocking also of the conditioned reflex to the partner stimulus. Matters, moreover, may and often do progress so far as to inhibit dramatically even the own inborn reflexes elicited by either partner stimulus (Struchkov).

Other facts obtained in our laboratory argue for the close interaction of forward and backward connexions. After establishing two-way conditioned reflex by pairing a paw movement with the blinking reflex it can be often seen that the unconditioned local paw movement induces unconditioned blinking, followed by the appearance of conditioned blinking (Varga and Pressman). The case is obviously one of circulating excitation between two cortical points through the medium of a two-way conditioned connexion between them.

The same phenomenon occurs in conditioning alimentary reflex to the light of an electrical lamp hung in the chamber. During the stage of specialization and consolidation of the conditioned reflex the animal almost never turns to the light and performs the proper food conditioned reflex. But, the delivered food consumed, he turns his head distinctly to the lamp, sometimes several times in succession, though the latter has already been turned off (Rudenko). A similar fact was received in establishing the two-way conditioned connexion by pairing light with sound and by testing the application of the first stimulus out of their combined pair (Davydova).

We have gathered considerable factual material suggesting the specificity of backward connexions studied by us and providing us with additional proof of their identity with the conditioned-reflex category rather than the phenomena of the type of Bahnung, dominant or facilitation type. Just as in chamber experiments, so also under the conditions allowing free movement of the test animals, it has been distinctly possible to elaborate simultaneously two heterogeneous instrumental conditioned reflexes. Flexion of either paw ensures food delivery and flexion of the symmetrical paw the delivery of water; or else flexion of one paw is followed by milk introduction into the mouth and flexion of the symmetrical paw by the cessation of a diluted acid flow into the mouth; or finally, flexion of one paw causes food to appear in one food bowl and flexion of the other paw brings food in the other. In all the various trials the activation of conditioned connexion as the experimenter presented the substances to their respective locations resulted exactly in the appropriate movement for each substance (Kolotygina, Popova, Rudenko, Struchkov).

We regard the factual data discussed above as direct experimental proof for the validity of the hypothesis by Pavlov and other scholars regarding the existence of the two-way conditioned connexion, moreover of its Pavlovian version, because either of the paired stimuli acquires the property of conditioned elicitation of the specific inborn reflex of its partner stimulus. The facts attest also that two-way connexions are inherent in all, or at least the

basic, modifications of conditioned reflex, and not just one, their instrumental modification, as Pavlov assumed. From this, it transpires that the function he ascribed to backward conditioned connexion—that of performing instrumental reflexes and voluntary movements—however important it may be per se, is by no means the total role of the connexion in conditioned activity.

At present, there does not exist as yet a sufficient body of reliable, solid and adequate experimental facts to state positively what other functions are assigned to the backward conditioned connexion in conditioned activity. Nevertheless, even with the factual evidence presently at our command it would be legitimate to not only ask the question but to venture some related ideas that require, of course, further rigorous experimental checking and strict theoretical validation.

Our first and basic assumption deals with the relation of backward conditioned connexion to reinforcement.

As is generally known, Pavlov, the founding father of the science of higher nervous activity, set exceptional value upon reinforcement in this activity, suggesting for it a key role not only in the formation and establishing of conditioned reflexes, but in all their further fate as well. The question about the physiological mechanisms of reinforcement is still one of the unravelled segments in his teaching. The problem of reinforcement, including this point, is one of utmost relevance in the modern research devoted to acquired activity of the brain.

It is not possible here to discuss the related experimental and theoretical studies, much less because they are conducted on a broad scale and from different perspectives. Let us just note that our opinion outlined here is so far a lone dictum, an assumption that presumes backward connexion to be the nucleus, the key element in the physiological mechanism of reinforcement, the structural and functional basis of performing the potent influence of the reinforcer brought to bear on the course and developmental pattern of conditioned reflexes and conditioned activity in its entirety. We consider supplementary the humoral and collateral nervous factors mobilized therein.

Our facts on the earlier formation of direct connexion suggest clearly that in the initial conditioning stage, i.e. the phase of generalization, the temporary connexion between excited cortical points establishes primarily in its early existence by the laws of Bahnung, the dominant and similar occurrences and approximates them in its specific features.

So far it has been somewhat difficult to state with certainty what general neurophysiological regularities govern the appearance of backward connexion between the same points (though we do have

some ideas about this). It is certain, however, that as the connexion appears it signifies the birth of a genuine conditioned reflex different in quality from the above-mentioned, non-specific and transitory phenomena. This even sets the stage for the circulation of excitation between two activated cortical points, an increase in the level of activity at these points and extension of the latter's retention time. All this makes it seem as though the above cortical points stand out prominently against the general background of its other parts, thus establishing a particularly favourable situation for potentiation, consolidation, and specialization of the two-way conditioned connexion that arises between them. This assumption is supported, though not in full, by our facts referred to above with regard to the circulation of excitation between the cortical points of paired stimuli joined together by two-way conditioned connexion. In this respect there is a certain interest in the findings of our experiments with the recording of multineuronal activity at the cortical points of the paired stimuli before and after reflex conditioning. A subsequent statistical analysis of connexions between the neurons of the two points of a Plurimat S-400 computer, by plotting cross-correlograms, showed a significant increase in one- and two-way connexions between the neurons of those two points, mainly at the expense of enhanced backward conditioned connexions (see Fig. 9.2).

Our viewpoint offers a clearer notion of the physiological mechanism for the development of internal inhibition in conditioned reflexes. With omission of reinforcement in some or other form, the cortical point of the reinforcing stimulus and backward conditioned connexion are deprived of their basic source of excitation, while their conditioned excitation through the medium of forward connexion alone, by repetitive action only of the conditioning stimulus, attenuate gradually, leading first to the blocking of the backward conditioned connexion. Our data on the greater inhibitability of backward conditioned connexions lend some credence to the suggestion.

With respect to the traditional conditioned reflexes elaborated by the so-called indifferent distant stimuli in combination with the biologically meaningful ones, the heightened excitability of the cortical points of the conditioning stimuli through the activation of backward connexion also has a special and biologically meaningful implication—to increase the sensitivity to near and distant stimuli giving out an advance signal of specific objects or events vitally important for the organism.

In conclusion, a few words will be in order on the point raised in the title of the present paper, namely, the universality of two-way

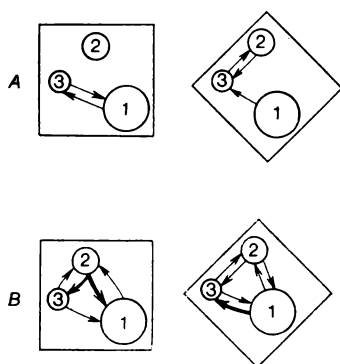


Fig. 9.4. A picture of connexions between cortical neurons in the visual (to the left) and sensory motor (to the right) regions.

A—before and B—after 'local' conditioned reflex elaboration (after Merzhanova, 1977)

connexions as applied to the reflexes acquired in individual life. This assumption is extensively documented by our data already cited to the effect that for higher animals two-way connexion is inherent in all of the examined conditioned-reflex varieties.

Two special facts greatly strengthen this argumentation. A genuine conditioned reflex was elaborated in the snail (*Helix lucorum*) by pairing food delivery with tactile stimulation of a certain body part inducing protective contraction of the pneumostom. Objective graphical

recording of the paired reflexes in their effector manifestation and the electrical activity of their respective command neurons identified the resulting reflex as a two-way reflex by virtue of having a two-way connexion (see Fig. 9.3). In our laboratory we have been concerned for years with a macro-electrophysiological study of a phenomenon we call local conditioned reflex. Our recent micro-electrophysiological investigations established a fact very relevant to the present discussion. As has already been noted, recording the electrical activity of the neuron groups at the cortical points of the paired stimuli has brought the realization that conditioning is marked by radical changes in the nature and interaction pattern of the neurons at these two points. In the same experiments another fact has been obtained: conditioning with a distant connexion also sets in motion a series of fundamental changes in the nature of the connexion and the interaction between the neurons at each of these cortical points, again with dramatic prevalence of two-way connexions (Fig. 9.4).

The assumption about the universality of two-way connexion for all forms of reflex activity of the nervous system, including its in-born forms, is supported primarily by logical argumentation. The concept of interaction between different parts of the central nervous system, both vertical and horizontal as well as between different reflexes, has long since been current in neurophysiology and

has become axiomatic. In the structural-functional language of modern neurophysiology this means that the interacting formations are linked with each other via a two-way neural connexion. Details relative to a specific substrate, trajectory, degree of complexity and other particulars of the connexion are of no major consequence in this case. For, as we shall attempt to demonstrate below, an essential role in the mechanisms of motivated behaviour belongs to the interaction of forward and backward conditioned connexions.

## **9.2. REFLEX MECHANISMS OF MOTIVATED BEHAVIOUR**

While still conducting his classical studies in the physiology of digestion the great Russian scientist Ivan Petrovich Pavlov used to say that science progressed by forward jerks, in step with advances in techniques. This has become a generally accepted truth. And the developments of the past few decades in the field of experimental research of the so-called motivated behaviour problem may be seen as new spectacular proof to the validity of this position.

As is known, the problem, though under different names and aspects, has long since been successfully approached in experiments by a number of prominent psychologists and brain physiologists, among them Thorndike, Pavlov, Köhler and their followers. The development of experimental research on the problem of motivated behaviour received a powerful impetus thanks to the design, improvement and widescale application of new methods permitting a direct, comprehensive and detailed inquiry into the functions of not only superficial, but also deep-lying formations of the brain in chronic experiments on animals (see the review of Doty, 1969) and clinical observations on patients. Through stimulation of the formations in question, recording of their electrical activity, their local electrolysis, and a host of similar techniques, workers in many countries, first and foremost in the United States, have secured experimental material whose formidable scope, diverse character, originality, and major scientific value place it in the same class as the most important break-through in the science of cerebral activity.

These successes, however, had also some negative consequences. In particular, the problem has been significantly divorced from the total body of knowledge about brain functions while many of the previously known facts and theoretical propositions of trend-setting significance in the behaviour of highly advanced organisms were ignored, if not totally consigned to oblivion. This was the case, in



particular, with Pavlov's accurate, wealthy, original and uniquely valuable factual data on the activity of the brain and his teaching of higher nervous activity, both virtually tantamount to an epoch in the evolutionary history of our knowledge about the functions of this supreme organ of the central nervous system. This inattention and negligence, and indeed occasional downright denial of the precious scholarly heritage in the field of research concerned with brain functions, were bound to be as detrimental in their consequences as has been a certain measure of alienation or self-isolation, so to say, of the motivated behaviour problem from the mainstream of current research into other cerebral activities. In sum, the various conflicting ideas of many aspects of the problem formed a background in which the overriding tendency for rejection of the reflex genesis and nature of motivated behaviour figured prominently, toning it down to a variety of non-reflex cerebral activities, most of which are activated and regulated by endogenous factors. The tendency in a milder form was embodied in the assumption of non-reflex and supra-reflex cerebral activities as primary agents of motivated behaviour, leaving to reflexes a secondary and auxiliary role.

It should be noted that most of the supporters of such concepts have lapsed into the bad tradition of marshalling the arguments and advocating their viewpoints, an altogether legitimate stance, in conjunction with the misrepresentation, indeed distorted explication of the essence of reflex theory and caricatured portrayals of the reflex, in general the conditioned reflex. Thereby the related scientific debate is stripped of its progressive significance and usefulness and reduced to a source and medium of misinformation.

In dramatic contradiction with the truth and Pavlov's authentic formulations, conditioned reflex theory is qualified as an analytical theory and one whose overall failure to consider the importance of the initial functional state of the brain, endogenous factors and previous individual experience of the organism, and the correlating effect due to the results of the actions performed by the mechanism of backward connexions is said to render it useless for understanding synthetical acts and self-regulation occurrences in the activity of the brain. Proven facts are ignored that postulate the existence of a large family of varied conditioned reflexes, different from one another in their degree of complexity, level of perfection, functional architecture, way of signalling, extreme dependence on endogenous shifts and external factors, well-pronounced adaptive variability and capacity for integration into complex forms of behavioural acts. Opponents of reflex theory persistently describe conditioned reflex as a monotonous, clichéd, automatic, rigid and non-variable phenomenon in cerebral activity.

I have the honour and fortune to be a pupil of I. P. Pavlov's and a staunch proponent of his teaching about higher nervous activity (or behaviour) which epitomizes the profound, evolutionary and dynamic comprehension of the reflex principle. Together with my co-workers I have been concerned over a long period with the experimental and theoretical elaboration of some of the key provisions of this teaching, including those which could, in the narrow sense, be referred to the so-called problem of motivated behaviour. The results of our investigations and critical analysis of the experimental and theoretical development of the problem of motivated behaviour allowed the conclusion that the Pavlovian teaching, of which it is in essence an integral component, provides it with the most solid and progressive theoretical basis. In the light of this teaching not only many tangled issues can be unravelled with maximum credibility, but the best prospects gained for a further successful development, both theoretical and experimental, of the problem of motivated behaviour as a whole.

One would like to do justice to a group of noted progressive investigators of the problem such as Miller (1941), Hull (1943), Delgado (1954), Cohen et al. (1957), Roberts (1958 [b]), Cofer and Appley (1964), Lissak et al. (1966), Morgenson and Stiven-son (1966), Bindra and Campbell (1967), Fonberg (1967), Milner (1970), Wyrwizka (1972), Valenstein (1972). In their experiments on different animal species they showed the essential, indeed sometimes decisive, contribution of environmental factors in producing various types of motivated behavioural acts and the involvement of the conditioned-reflex mechanism in their formation and performance. This was an important step forward in the use of the Pavlovian idea to gain insights into certain particular aspects of the problem at its current stage of elaboration, aided by up-to-date experimental techniques. Yet these studies, however significant, should be seen as only the first steps in that direction. Let alone the fact that some of them examined the role of the conditioned reflex mechanism in motivated behavioural acts within a limited scope, on a relatively low methodological level, and in a somewhat primitive form, it ought to be emphasized additionally that the Pavlovian teaching holds a number of other theoretical concepts and ideas receiving no attention from investigators, which may nonetheless provide fruitful and effective ways for the experimental and theoretical treatment of many intricate points associated with the motivation problem.

In recent years we attempted in a series of publications in Russian and foreign languages (1974, 1976[a], 1976[b], 1977, 1978) to validate the statement above with pertinent facts—either those obtained by numerous other researchers or coming from our laboratory, and arrived at certain theoretical conclusions.

A reminder should be given that Pavlov visualized in higher nervous activity or behaviour a great deal more than merely conditioned reflexes or other acquired reflex forms, as some researchers would have it. His definition of this activity as one that ensures the most perfect regulation of the organism's exceedingly complicated relationships with the environment stated it to be a product of interconnected activity by the cerebral cortex and subcortical formations; it was also said to consist of several instances each different in terms of genesis, character of its constituent reflexes and the anatomical substrates that put it into effect. By the first instance, he meant specialized, exceedingly complex unconditioned reflexes—alimentary, defensive, sexual, etc., otherwise known as instincts, drives and the like, which he thought of as the reflexes effected mainly by subcortical formations. The second instance he understood as the conditioned reflexes elaborated on the basis of the just mentioned unconditioned or inborn reflexes; he considered them to be the principal type of acquired reflexes and the cerebral cortex to be their substrate in higher animals and man.

There can be no doubt that he would have classified in the same instance associations, the newly acquired reflex type, he discovered in anthropoids in the latest period of his life; these he placed above ordinary conditioned reflexes. The two instances, Pavlov assumed, accounted for the whole higher nervous activity in animals. In man, however, he conceded over and above those two, a third instance of higher nervous or psychic activity specific to man alone, in the form of a verbal or second signal system of reality whose substrate he likewise identified in the neocortex.

According to Pavlov, the involvement of subcortical formations in behaviour was not limited to supporting the relative independence of the enormously complicated and vitally important alimentary, defensive, sexual and other unconditioned reflexes accomplished by them, nor to the latter's role as the basis for the elaboration of corresponding conditioned reflexes. He believed in the continuous tonic influence by these formations on the cortex, increasing its activity potency. Furthermore, with respect to the subcortical formations, Pavlov emphasized strongly the exceptional value of the initial functional state of cerebral structures for their activity and the major importance of endogenous factors, both nervous and humoral, in modifying their functional state.

It is clear from the foregoing that the Pavlovian teaching of higher nervous activity, based wholly on the principles of reflex activity, can serve as a solid scientific basis for the correct comprehension and interpretation of the behavioural reactions known as motivated; it contains, moreover, all the necessary elements which common judgement regards as characteristic of and specific to motivated behaviour. This applies, in particular, to the relation of the subcortical

formations and endogenous humoral factors to such behaviour, although for reasons well-understood Pavlov's reference to it at the time could not be other than general, global, and without the extent of detail and specificity which mark the present status of knowledge about the problem of motivated behaviour.

The great potential of the Pavlovian teaching for the effective management of the motivated behaviour problem can be instanced by a more satisfactory explanation of the abundant, reliable and valuable factual data on some node points of the problem than we feel is achievable from the perspective of other theoretical concepts.

We shall discuss here three such questions, namely: (a) whether the same behavioural act can be produced with electrical stimulation of different deep brain structures and whether conditioned reflexes can be elicited through such stimulation either as reinforcement or a signal; (b) whether behavioural acts of different types can be evoked with electrical stimulation of one and the same formation; (c) goal-directed character of motivated behavioural acts.

The current differences of opinion over each of the points are well known and therefore need not be reiterated here.

From the viewpoint developed here and given the present state of the problem, the best way to grasp the essence of the first point is to examine the above-mentioned substantive Pavlovian concept regarding the instances of higher nervous activity in conjunction with his perception of nervous centre. He saw it as an assembly of nervous structures broadly spaced in different parts of the brain or below it, closely connected with one another, comprising a single complex whole, structurally and functionally, and performing a definite function. These ideas, together with the consonant notions of Magnus (1924) and Sherrington (1948) about different in-born reflex integration levels, and our experimental results (we studied the influence of surgical removal or functional shutoff of the cerebral cortex in higher animals on the state of different unconditioned reflexes and the organism's functions) formed the basis of our hypothesis (1955) on the multi-storied architecture of the arc of inborn reflex or nervous centre, and its schematic representation (Fig. 9.5). Later on we also employed this idea and the scheme in our work on the problem of motivated behaviour, and in particular our attempts to understand and interpret the phenomena mentioned above. And, we become increasingly aware of their even greater adequacy here than elsewhere.

We believe that the branches of the central part of the unconditioned reflex arc (I-V) passing at different levels of the central nervous system are neither equivalent structurally and functionally, nor play a similar role. Each branch is distinguished by its own

structural and functional features and imparts a specific functional shade to the respective reflex. The main branch of the reflex arc of each type, the determinant of its principal features, runs at one level among their hierarchical series in the system levels. Since the arc of many elementary motor and vegetative reflexes has its main branch within the spinal cord (level I) and for the arc of complex cardiovascular, respiratory, tonic cervical and labyrinthine

reflexes it occurs in the medulla oblongata (level II), there is sufficient reason to believe that the main branch of the most intricate alimentary, drinking, sexual, aggressive and other unconditioned reflexes of interest is found within the hypothalamus (level III).

This being so, the structures of the various limbic formations, implicated in these most complex specialized unconditioned reflexes, could perhaps be viewed as satellite or supplementary relative to the hypothalamic branch and are located in the area of levels III-IV. The cortical branch of the arc of each reflex (level V),

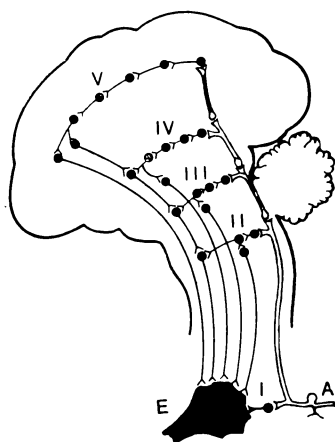


Fig. 9.5. Diagram of conditioned reflex arc.

I-V—branches of the central part of the reflex arc on different levels of the central nervous system. A—afferent neuron, E—efferent neuron (after Asratyan)

however, is identified with what Pavlov termed cortical representation of an unconditioned reflex, maintaining high perfection of its realization and forming the basis for the many and varied conditioned reflexes to all possible stimuli from the outer world and to diverse endogenous stimuli.

In the light of such a concept the facts of many authors (Hess, 1949; Robinson and Mishkin, 1962; Morgane, 1969; Anand, 1971; Valenstein, 1972, and others) state that by electrostimulation of the hypothalamus and many formations of the limbic system (hippocampus, amygdala, septum, and cingulate gyrus) it is possible to evoke a particular inborn or motivated act, whether alimentary and drinking, or aggressive, sexual, etc. They are thus understood by us as resulting from the activation of some elements, to be found in each of the formations, of the composite arc of some particular one amongst those most complex, specialized unconditioned reflexes.

The possibility of elaboration on the basis of their stimulation, as a reinforcing factor, of conditioned reflexes to a situation or to individual stimuli (Cohen et al., 1957; Roberts, 1958[a]; Miller, 1961; Delgado, 1964; Fonberg, 1967; Mogenson, 1972; Bindra and Campbell, 1967; Gangerelli, 1975) is also easy to understand from this viewpoint. Their stimulation unavoidably excites also the cortical branch of the appropriate unconditioned reflex arc. With simultaneous stimulation of the cortical points of the situational factors or special stimuli, an appropriate conditioned reflex is elaborated.

The facts concerning the elaboration of conditioned reflexes to electrical stimulation of hypothalamic structures and some formations in the limbic system as a signal or a conditioning stimulus can be more satisfactorily comprehended and interpreted from the viewpoint developed here (Mogenson, 1962; Nielsen et al., 1962; Ellen and Powell, 1966; Asratyan, 1977).

It should be noted that until recently the experimental data on this point have been much inferior in quality and cogency to the data underlying the other of the phenomena discussed above. This was because some inadequacies of experimental conditioned-reflex research common, much to our regret, for the relevant studies by our many foreign colleagues, were most in evidence in this area. Our concern here is with the way these reflexes were examined by methods much too inadequate for the standards developed in Pavlov's laboratories.

For one thing, the experiments carried out mainly on rats did not involve any objective graphical recording of the established conditioned reflexes with their principal characteristics, such as latent period, magnitude, character, duration, etc. For another, the inquiry into question under discussion here followed, on the whole, a sophisticated plan. In most of the investigations the phenomenon of self-stimulation had been pre-conditioned in a special series of trials, next the habit of pressing a lever to get food was formed in another trial series on the same animals, and then in a third trial series the self-stimulation points (or reward stimulation, to use the authors' term) were paired either with food obtaining or with electrical stimulation of the paws by the shuttle box method with an aim to elaborate in them the proper alimentary or defensive conditioned reflexes. Some conclusions about the relationships between the phenomena of self-stimulation and conditioned reflex might be deduced from the findings of the similar experiments. Yet it would be an uphill task to look to them for a clear-cut and unequivocal answer to the question whether the conditioned reflexes to electrical stimulation of deep brain formations can be elaborated as a conditioning or signal stimulus.

From the studies of other authors on the same subject we should like to single out only those carried out on cats by Nielsen et al.

(1962) as more or less satisfactory both in methodology and the results obtained. In chronic experiments on cats having each over 20 electrodes implanted in different deep brain formations, including some limbic structures, by pairing electrical stimulation of some of the formations with local electrical painful stimulation of one of the animal's forepaws they have succeeded in elaborating an instrumental defensive conditioned reflex of the avoidance reaction type.

Over the past few decades a large group of our laboratory staff have been engaged in the experimental study of the problem. Alimentary and defensive conditioned reflexes, both classical and instrumental, were elaborated in cats and dogs, using direct electrical stimulation of different subcortical formations as a signal or conditioning stimulus. The job involved objective graphical recording of all needed parameters and close compliance with all of the strict rules developed by Pavlov for the elaboration and study of conditioned reflexes (Asratyan, 1970). In this regard, a much stronger emphasis has recently been placed on hypothalamic nuclei and some formations of the limbic system. We believe that the results obtained are unquestionable proof that alimentary and defensive conditioned motor reflexes to electrical stimulation of these deep formations as a conditioned stimulus can be elaborated. Presented in brief outline, their gist is as follows.

The experiments were carried out on dogs and cats with chronically implanted electrodes into the nuclei of the hypothalamus (lateral and ventromedial), amygdala (lateral, cortical, and basal), septum (lateral and medial) and hippocampus (dorsal and ventral regions). In the dogs, local instrumental conditioned reflexes, alimentary and defensive, were elaborated in the traditional insulated sound-proof chambers and objectively graphically recorded simultaneously with some other essential functions of the organism. The cat experiments were laid out in large insulated cages giving the animals unrestricted freedom of movement; in them, alimentary conditioned reflexes were elaborated and objectively graphically recorded either as directional advance to the feeder or a local instrumental food-procuring movement.

As part of the program, evoked potentials were also recorded at the cortical points of the 'instrumental' paws. To stimulate the deep brain formations, two-phase rectangular current of moderate intensity (0.2-0.8 mA) was supplied at 10-100 Hz frequency for the stimulation time of 2-6 seconds. In other experiments conditioned reflexes to traditional external stimuli were elaborated in the same animals, along with the conditioned reflexes of the kind mentioned earlier.

The factual data obtained from these experiments are partly illustrated in the figures below; they show that both alimentary, and

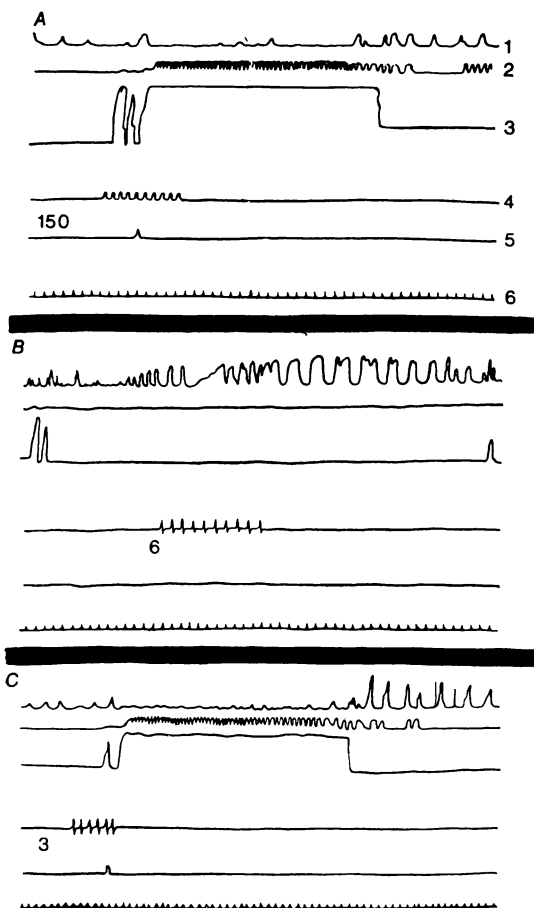


Fig. 9.6. Alimentary instrumental conditioned reflex in response to electrical stimulation of septal medial nucleus in the dog.

A—elaboration of conditioned reflex; B—extinction of the conditioned reflex; C—restoration of the conditioned reflex. Figures below the stimulus mark indicate the number of stimulus-reinforcer pairings (A and C) or the number of stimulus presentations without reinforcement (B). Top down: recording of respiration, chewing, paw movement, septum stimulation, food bowl delivery, time in seconds (experiments of Balezina, 1981)

defensive instrumental conditioned reflexes, either general motor or specialized local motor, can be elaborated in response to electrical stimulation of the above-mentioned deep nervous formations. Of these, homofunctional conditioned reflexes (e.g., alimentary con-



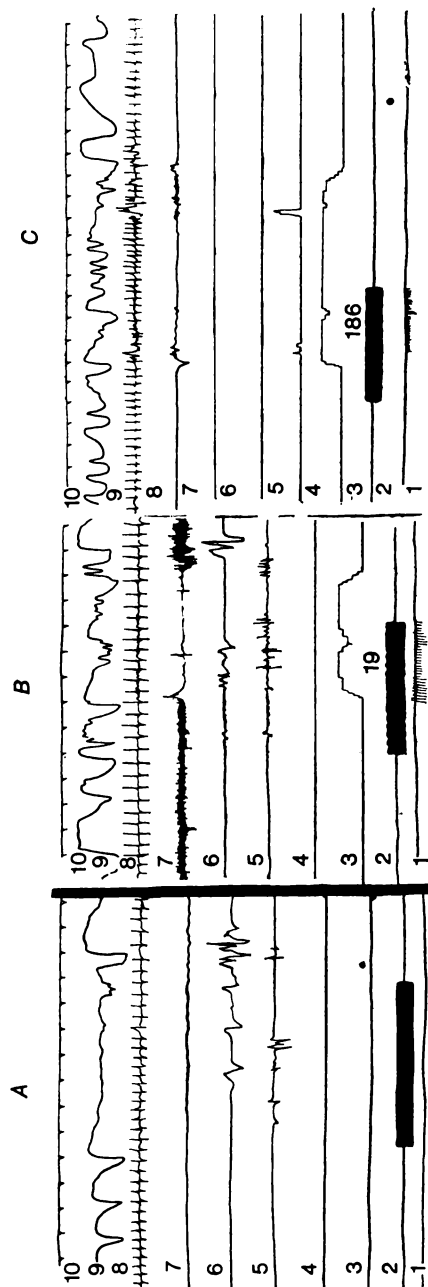


Fig. 9.7. Elaboration of defensive instrumental conditioned reflex to electrical stimulation of lateral hypothalamus in the dog.

A—before conditioning; B—conditioning stage; C—conditioned reflex stage. Bottom up: 1—unconditioned stimulation (short strokes denote electrocutaneous stimulations switched off by paw raising); 2—conditioned stimulation (the figures indicate the number of pairings); 3 and 4—mechanograms of the left and right paws; 5—recording of head movements; 6—mechanogram of chewing movements; 7—EMG of the left forepaw; 8—ECG; 9—respiration; 10—time in seconds (experiments of Chilingaryan)

ditioned reflexes to electrical stimulation of the lateral hypothalamic nucleus) are elaborated more rapidly and easier than heterofunctional conditioned reflexes (e.g. alimentary conditioned reflexes to electrostimulation of the ventromedial hypothalamic nucleus). From our data it is inferrable that by the dynamics of their formation, specialization and consolidation these reflexes hardly differ in principle from conditioned reflexes to external outside stimuli. They take 20 to 30 pairings to appear and 50 to 70 pairings to become stable, their latent period decreasing gradually (Fig. 9.6, 9.7, 9.8, and 9.9).

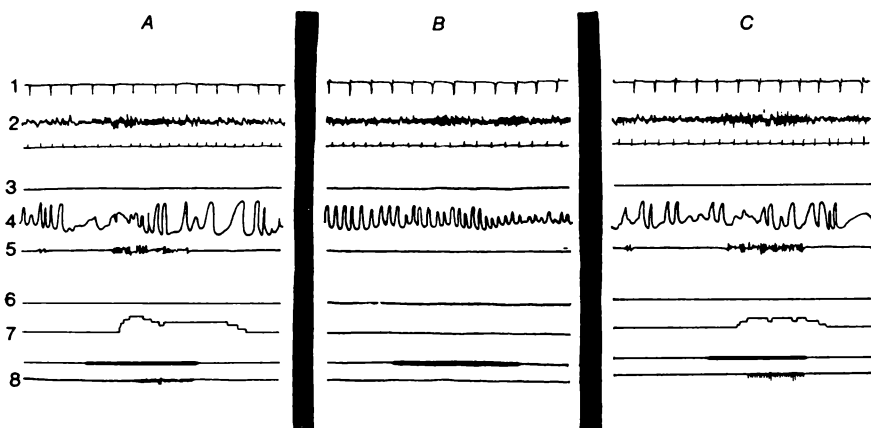


Fig. 9.8. Defensive instrumental conditioned reflex to electrical stimulation of ventral hippocampus in the dog.

A—conditioned reflex; B—extinguished conditioned reflex; C—restored conditioned reflex. Top down: 1—time mark; 2—electrical hippocampal activity; 3—ECG; 4—breathing; 5—head movement; 6—mechanogram of the left forepaw; 7—mark of conditioning stimulation; 8—unconditioned stimulation (experiments of Grigoryan)

Significantly, as the stimulations of these formations become a signal for food or defensive activity, the inborn reactions they initially evoked tend to be gradually inhibited and disappear. This shows up most vividly whenever the initial reaction to electrical stimulation of a formation is of a defensive-aggressive character, as, for example, in the stimulation of the ventromedial hypothalamic nucleus or the lateral septal nucleus, and such stimulation results in alimentary conditioned reflexes. With time, the defensive-aggressive reactions to the similar stimulation attenuate, disappear and give place to a distinctly manifest, general motor food reaction and local alimentary instrumental motor reflex. One cannot help noticing some similarity between these data and the results of the well known experiments of Erofeeva

in Pavlov's laboratory, in which conditioned alimentary reflexes to electrical painful stimulation of the dog's paw were elaborated.

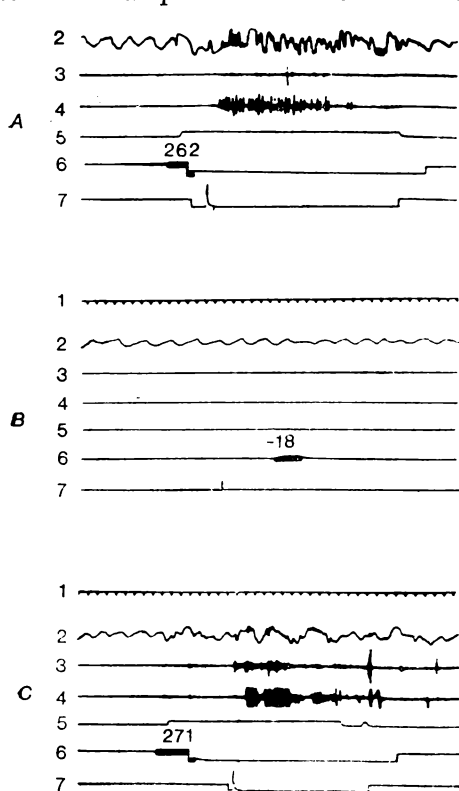


Fig. 9.9. Alimentary conditioned reflex to electrical stimulation of lateral amygdala nucleus in the cat.

A—established conditioned reflex; B—extinguished reflex; C—restored reflex. Top down: 1—time in seconds; 2—breathing; 3—the left eye blinking; 4—chewing movements; 5—head turn to feeder; 6—stimulation mark (shaded line segment); leaving of the start platform and re-entry after feeding; 7—approach to feeder and departure from it. The figures indicate the number of pairings and of non-reinforced stimulations during the course of extinction (experiments of Daurova and Kolotygina)

Once established, these conditioned reflexes are extinguished and restored (see Figs. 9.6, 9.7, 9.8, and 9.9); they are generalized both within the limits of the given deep formation, and also by embracing other formations, and differentiations to them can be elaborated in either case.

The physiological mechanism of conditioning to electrical stimulation of the above-mentioned deep cerebral formations as a signal or conditioned stimulation is as follows. In essence, any primary conditioned reflex may be considered as a result of paired activity by two unconditioned reflexes, as a product of their synthesis. The formula is as valid for the instances of pairing a so-called indifferent stimulus (the orientation reflex caused by it is also unconditioned) with some biologically meaningful stimulus, as it is for the cases of pairing two typical unconditional stimuli, as exemplified by the just mentioned experiment of Erofeeva (Pavlov, 1973). It is obvious that the power correlations of the

paired stimuli, their order of action and other factors mattered a great deal in it.

As previously described, in our experiments the cortical branch of the arc of one of the unconditioned reflexes is activated by stim-

ulation of the subcortical elements of its own arc with moderately intensive current. This is followed by a still stronger stimulation of the cortical branch of another unconditioned reflex, alimentary or defensive, through natural stimulation of its receptive field. Thus the basic conditions are made available for the elaboration of the appropriate conditioned reflex.

Our conceptions about the effectiveness of creative use of Pavlov's other ideas and theoretical propositions for proper and strictly scientific comprehension and explanation of other issues related to the problem of motivated behaviour will be outlined below in a synopsis, because they have been set forth time and again in our previously mentioned publications (Asratyan, 1973-1978).

The second of the questions listed above refers actually to the facts established by many researchers that by electrical stimulation of one and the same point of one and the same nucleus of the hypothalamus or some limbic formation it is possible to elaborate most diversified motivated behavioural reactions, either alimentary, drinking, aggressive or sexual, depending on the change in the intensity, frequency or other parameters of the stimulating current, functional state of the organism or situational factors of the experiments (Roberts, 1958 [a, b]; Mogenson and Stevenson, 1966; Grastyan et al., 1966; Qallistel, 1969; Caggiula, 1970; Mogenson, 1972; Valenstein, 1972; etc.). These facts work patently against the traditional concept regarding static specialization and localization of functions in the central nervous system of highly developed organisms. They are nevertheless easy to understand and interpret if approached from the concept of dynamic specialization and localization of functions with special reference to the cerebral cortex proposed by Luciani (1915) as a sketch, further developed in detail by Pavlov (1973) as a clear-cut theoretical proposition, and expanded by us (1949) to the entire nervous system as a general principle.

Essentially, the concept features the assumption that the morphological substrate of specialized functions has the form of representation as limited nuclear zones holding each a concentration of the nervous elements that are highly specialized for a given function, or as extensive peripheral areas with less specialized dispersed nervous elements which are represented there in order of decreasing density. The areas of dispersed elements overlap to form a peculiar polyfunctional mosaic of structures. Unless hypothalamus and other formations in the limbic system are an exception to this rule, it is easy to understand that electrical stimulation of their individual points simultaneously embraces in varying degree the structures of several specific functions and either activates them discretely and at different times, depending on the level of excitability and parameters of the stimulating current, or increases

their excitability all at once, thus establishing a potentially favourable situation and making them readily available for the activation of any one of them given an adequate external stimulus in the environment.

It should be pointed out that a similar viewpoint but from a slightly different positions is put forward nowadays also by some other researchers (Millner, 1970; Mogenson, 1972; Valenstein, 1972).

The third node point of the problem of motivated behaviour, which we are trying to approach from novel positions, is concerned with the goal-directed character of motivation. It is generally accepted that goal-directedness is the most typical feature of motivated behaviour, while its interpretation is the most confused issue of the problem. Statements about this question are either of the character of free expression in a teleological spirit, reduced to a simple description of the phenomenon itself, or an enumeration of the presumed circumstances and factors underlying the goal-directedness of the behaviour. For example, the goal-directed nature of motivated behaviour is ascribed to the 'cognitive map' developed in an animal's individual life (Tolman, 1948) to the guiding influence of the so-called 'psychonervous image' (Beritashvili, 1960), to the presence in the brain of 'predictive cell clusters' whose activity is corrected by sensory signals (Milner, 1970), to the primordial existence of a goal and the programming role of the so-called 'action acceptor' (Anokhin, 1968), to the action of environmental factors acquired by training with a certain orientation value (Bindra, 1974), and to the development of complex systems of 'sub-goals' in the process of accumulation of individual experience, and their consecutive realization with account taken of the results of each covered stage (Deutch, 1960). Unable as we are here to comment on these views in much detail, we shall nearly point out that the majority of them, as we see it, give no clear or straightforward answer about the physiological mechanism of the phenomenon itself as it stands.

Basic to our viewpoint on the essence of the matter in hand is Pavlov's idea about two-way conditioned connexion, the idea he stated hypothetically with special reference to the instrumental variety of conditioned reflex. He believed that the elaboration and performance of an instrumental movement are stipulated by the formation and activation of backward conditioned connexion. Considering that many researchers justifiably see in instrumental conditioned reflexes a rather suitable investigative model of motivated behaviour, it becomes clear that the new interpretation of the reflex's physiological mechanisms suggested by Pavlov came so handy for effective use of the model to provide key insights into the physiological mechanisms of motivated behaviour in its entirety.

We seized the opportunity boldly and enthusiastically also for another reason. This was because the teacher's idea was followed up in many-year systematic studies by his followers, first of all ours with associates (Asratyan, 1970, 1977) and of a Czech scholar Dostalek (1964). As a result, it has grown by now into a theoretical proposition fairly well grounded experimentally.

More specifically, this is what we talk about.

In the procedure of instrumental conditioning there is a certain movement that always comes ahead of reinforcement to become

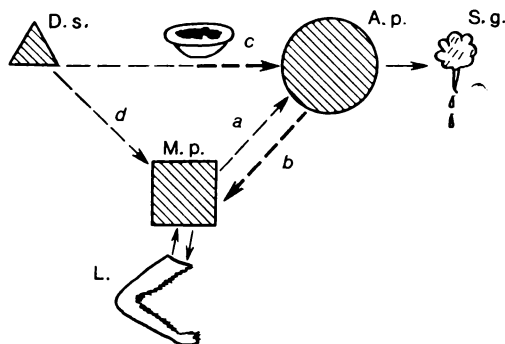


Fig. 9.10. Diagram of alimentary instrumental conditioned reflex. D.S.—distant conditioned stimulus; A.p.—cortical point of food unconditioned reflex; M.p.—cortical point of the paw. L—the paw, S.g.—salivary gland; a, b, c, d—conditioned connexions (after Asratyan)

a signal stimulus capable of eliciting a reinforcing reflex conditionally through a direct conditioned connexion. It is legitimate to assume, as Pavlov did, that the performance of this movement as a result of food excitation caused by endogenous or exogenous factors is stipulated by the activation of the backward connexion established by this procedure, i.e. from the food centre to the cortical structures of the instrumental movement.

On the basis of the extensive and diversified factual materials on that subject gained in our laboratory and guided by this idea, we proposed many years ago (1966) a schematic representation of the arc of such a reflex (Fig. 9.10). We feel that this scheme may provide a key to proper understanding of the physiological mechanisms that underlie the generally known models of instrumental reactions, as they do also the phenomenon of self-stimulation (Olds and Milner, 1954). Aided by the scheme and in the light of its underlying concept, one will find it easy to understand and interpret adequately also facts of another kind. With alimentary, drinking or protective instrumental reflexes pre-conditioned in test animals, the subsequent electrical stimulation of hypothalamic structures from the locus at once elicits the established instrumental movements as

well as the corresponding natural unconditional stimuli are able to do it (Grastyán et al., 1956; Andersen and Wyrwicka, 1957; Miller, 1961; Delgado, 1964; Wyrwicka et al., 1972).

We are inclined to explain postural training of test animals prior to performing the required local conditioned movement in the experimental environment of special cabins by the activity of backward conditioned connexion (Kasyanov, 1950; Joffe, 1957). Moreover, a thorough analysis of the facts obtained from the study of alimentary conditioned reflexes in dogs and cats under free movement about a spacious experimental room or a large cabin leads us to the conclusion that their established habit for prolonged stay on a certain start platform pending the next starting signal can hardly be better explained than as an expression of tonic activity by the same backward conditioned connexion. One is brought to that conclusion by the data of special experiments by our collaborators Struchkova, Rudenko, Davydova, Daurova, Kolotygina, Vanetsian, and Shumikhina (Asratyan, 1977), as much as by the facts of Kupalov (1964) with co-workers about the so-called situational conditioned reflexes. In both these series the test animals were not to be given food during conditioning unless they moved to the feeder right from the start platform. Because of this, the latter developed with time into a continuous spatial conditioned stimulus linked with the reinforcing stimulus through a two-way connexion.

Thus, in our scheme of things, the formation of two-way conditioned connexions and the activation of backward connexion are essential in the performance of the above-mentioned elaborated reactions which are, in effect, elementary goal-directed actions clearly with an adaptive purport.

From our point of view, these peculiarities of conditioned connexions are also essential in the mechanism of complex behavioural acts named motivational. Our assumption must not be perceived as mechanical extrapolation from the elementary to the complex. In the wake of Pavlov we regard complex behaviour not as a simple sum or superposition of elementary behavioural reactions upon one another, but as a product of the latter's supreme integration or synthesis into one whole with its specific features, a synthesis which lets the components retain their properties but only up to a point.

The validity of this fundamental Pavlovian theoretical concept was proved in as vivid a form as it was convincing in the experiments conducted by Pavlov and his co-workers to investigate behaviour in anthropoids (Pavlov, 1973). The experiments demonstrated, among other things, that the chimpanzee, to get hold of the objects suitable for satisfying his immediate needs, began to interact vigorously with the environment and by 'trials' and 'errors', and in agreement with underlying principles of conditioning, to grad-

ually elaborate and improve first easy and simple and then, through their integration, increasingly more complex and difficult habits and ended up forming a rather complex and long chain of integral behavioural acts. Here is an example of what the animal might do: the chimpanzee unlocked with a key the door to the cabin, entered it, put out the flame of burning spirit on a window sill, went through the window to a room next door with fruit hanging much too high for him, put up a steady pyramid from crates lying on the floor, climbed it and grabbed the bait.

At odds with the views of Köhler (1929) and other Gestalt psychologists, this theoretical Pavlovian concept was later proved convincingly by new experimental findings of his followers, especially Vatsuro (1948) and Schastny (1972). We presume that the fascinating factual evidence of Wolfe (1936) and other workers concerning the formation dynamics of the counterusing habit in anthropoids agree with the above theoretical concept of Pavlov, as are also the extremely interesting factual data of Ulanova (1950), the Gardners (1969) and other authors about the formation dynamics in anthropoids of the speech of gestures though the scientists themselves held a different view of their own facts.

For his analysis of the experimental data relating to the mechanisms of complex behavioural acts in higher animals, including also anthropoids, Pavlov made no use of his idea about two-way conditioned connexion. Originally formulated with reference to simple instrumental conditioned reflex, this profound idea had developed to date, as was noted earlier, into a theoretical proposition of its own, rested upon a sufficient body of experimental evidence. So we took it that the time had come to make careful steps in the direction of exploring a possible role of two-way conditional connexion in some other phenomena in cerebral activity with special reference to the physiological mechanisms responsible for the goal-directed character of motivated behaviour.

It makes no difference if the complex habit being formed in the animal is of the type involving selection of an adequate key to unlock the door, building a pyramid from crates, putting out a flame, raising the bridge over a water obstacle, using counters or the language of gestures—in all these instances the systems of specific movements performed in a certain sequence end up with the acquisition of and then reinforcement by the requisite, biologically meaningful objects.

It would be legitimate to assume the progression of things leading to it to be virtually the same as for the instrumental conditioning to a certain elementary movement. This is to say, complex chain conditioned reflexes are elaborated in response to appropriate systems of movements, because at all events they precede the reinforcement in time. As with elementary instrumental conditioned re-



flex, it is likewise conceivable, for each of the instances above, that a system of two-way conditioned connexions is formed. These are forward connexions, from the cortical structures of the system of movements (as a chain conditioned stimulus) to the cortical point of the reinforcing stimulus, and backward, from the latter to the former. If, after Pavlov, we deduce from considerable experimental

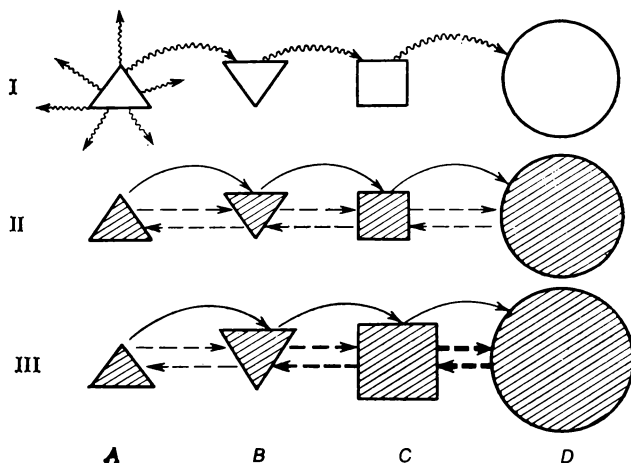


Fig. 9.11. Diagram showing physiological mechanisms of goal-directed behaviour. For the explanations see the text (after Asratyan)

data that local instrumental conditioned reflex, as a model of goal-directed voluntary movement or elementary motivated act, is a consequence of activation by backward conditioned connexion, then we would be right in assuming the goal-directedness of motivated behaviour to be largely a result of activation in the previously mentioned system of backward conditioned connexions.

In essence, our viewpoint on the subject of the discussion as regards the formation and performance of motivated behaviour by animals in their natural habitats, presented concisely, comes down to the following. A naive animal, to meet a current pressing need of its organism in an unfamiliar environment, is influenced by endogenous and exogenous factors into making a multitude of searching movements in all possible directions from the initial point (in Fig. 9.11 this is white triangle IA with its outgoing, continuous twisting arrows). While doing this, it may advance once or several times in a certain sequence through the intermediate nodal points of the route (white geometrical figures IA-IB-IC with unidirectional twisting arrows) to its destination—the location of the sought-for object (the white circle). If it does and if it can meet the

current pressing need, a chain of spatial-temporal conditioned reflexes with two-way conditioned connexions is formed among the cortical projections of the key points along the route (in Fig. 9.11 these are the thin broken arrows between shaded geometrical figures IIA-IIB-IIC-IID; they identify not just the key points along the effective route, but also their projections or 'images' in the cerebral cortex).

Even at the initial stage of their formation these conditioned reflexes are able to give the animal proper orientation so to enable it, without extra searching or wavering, to head along the route to the location of the required object (the unidirectional continuous arc-like arrows between the shaded figures).

Not so at the consolidation and specialization stage of the established chain of spatial-temporal conditioned reflexes—then two-way conditioned connexions and the conditioned reflexes they mediate grow in strength and power in keeping with the long-familiar regularities, as the animal approaches the location of the object and the time of reinforcement (IIIA-IIIB-IIIC-IIID).

We believe that the major driving force of this complex integrative system of conditioned reflexes in the form of an integral behavioural act is increased excitability or excitation of the central nervous structures of the reinforcing stimulus or the integrated nervous centre of the most complex, specialized and vitally important unconditioned reflexes in the Pavlovian sense. The latter's increased excitability or excitation ('central motivational state' in other authors) may be induced by both endogenous neurohumoral factors and by many varied distant or near signals, or conditioned stimuli ('acquired drive' or 'conditioned incentive motivation' in other authors). If activated in one way or the other, this integrated nervous centre sets in motion, in its turn, the entire complex integrated system of conditioned reflexes, chiefly through the medium of the chain of backward conditioned connexions that were established between its cortical representation and other motor and sensory cortical points along with forward conditioned connexions. This activation may take the form of increased excitability of nervous structures throughout this complex system getting them ready for work or alerting them for activity. Another form it can assume is of an excitation actuating complex reflex activity of the entire system as a whole.

One can also imagine immediate forward and backward conditioned connexions between intermediate points and the final destination but not illustrated on the diagram so as not to make it overly complex. For the same reason the scheme left out also the backward connexion from the cortical points of the vitally important conditioned reflex to the cortical points of the signal stimuli, known from the data of our laboratory to increase dramatically

the latter's excitability and thereby to have large implications for behaviour in its entirety.

At present we have a fairly modest body of our own experimental data which could be considered as direct substantiation of the standpoint just proposed.

The regular patterns of integration of separate conditioned reflexes into rather complex integral behavioural acts have recently been included by workers of our laboratory in the agenda of research under conditions of free movement of the experimental animals. As a specific methodological characteristic, these experiments involve objective graphical recording of the studied reflexes of the type generally practised for trials on animals fastened to the experimental table. In these experiments the process leading to elaboration of separate conditioned reflexes with two-way conditioned connexions and their integration into complex behavioural reactions were examined. It included conditioning of an instrumental alimentary reflex of pressing a lever, elaboration, on this basis, of a second-level conditioned reflex to an external stimulus, further complication of this chain by elaboration of a conditioned reflex to a spatial factor—prolonged stay on a certain start platform until exposed to some starting conditioned stimulus, synthesis of all hitherto available conditioned reflexes into a certain dynamic stereotype of behaviour, switching of the entire system of the conditioned stimuli from signalling one type of activity to another type, and so on (Davydova and Struchkov, 1978; Rudenko and Struchkov, 1978).

From the viewpoint of the physiological mechanisms of goal-directed character of motivated behaviour, which are of interest to us, our following data may be of special interest. The relationship, universally known since the time of Kendler's experiments (1946), between alimentary and drinking behaviour of animals and excitability of the central nervous formations controlling these functions was examined by Rudenko and Struchkov in the series of experiments on dogs briefly mentioned above. Two independent setups were built in a large room with a certain space between them. They shared some similar components: a short platform, a box with an in-built device for food and water delivery 4-meter-distant from it and a lever to press in order to get food or water, spaced at 80 cm from the latter. On the same dogs and in the same series of experiments a system of drinking conditioned reflexes was established on the first of these setups and a system of food conditioned reflexes on the second one. The respective starting signals were a musical tone for the drinking system of conditioned reflexes and rhythmical metronome ticks for the system of food reflexes.

Among the facts obtained from the experimental stage of reflex

specialization and consolidation the following deserve attention. With thirst pre-intensified in the dogs by water deprivation they would commonly rush, once in the experimental room, to the start platform for the system of drinking conditioned reflexes and stayed there until the starting signal stimulus came into action. Similarly, with pre-intensified hunger through food deprivation they would enter the room and go to the start platform of the food reflexes and remained there until the adequate starting signal came through. After a chain of movements were performed and reinforced with the appropriate food product they would return to their adequate start platform. If, however, satiety with either product was reached they would often move to an inadequate start platform. Some of the dogs experiencing very hard thirst or hunger would much rather stay near the adequate box instead of on the start platform; not infrequently they would run up straight to the adequate box without stopping to press the lever and did it after approaching the box. Simultaneous satiety with water and food led to disturbance of the reflex systems and confusion in deciding between the start platform as well as between the levers and boxes. On several occasions the dogs would merely wander about the room, coming up at times to one or the other of the boxes and pressing one or the other lever.

These facts reveal quite obviously the singular importance attaching to excitability of the central nervous structures of the most complex alimentary and drinking conditioned reflexes in the performance of appropriate behavioural acts, but not only that. To us, they would appear also to be suggestive of two-way specialized conditioned connexions that come up between the cortical elements of the structures associated with either unconditioned reflex and the cortical points of the systems of advance towards the appropriate start platform, lingering on it and pressing the appropriate lever. This applies to the formation of both, the forward conditioned connexions from the cortical points of these movements to the cortical points of each of the reinforcing stimuli, and the specialized backward conditioned connexions by whose activation the central nervous structures of the reinforcing stimulus actually elicit, for the most part, the above-mentioned goal-directed movements.

We see the data as a preliminary and more or less adequate experimental support for the expounded viewpoint on the physiological mechanisms for the goal-directed character of motivated behaviour.

We realize fully well that our ideas of the reflex mechanisms of motivated behaviour, outlined here, have much hypothetical and debatable about them and consequently need to be further explored in a consistent and thorough-going manner both theoretically and experimentally. We believe, however, that our proposed concept, even as it stands now, compares favourably, with the current, half-

way and eclectic and sometimes also teleological concepts because it is seeking to transport the question about the mechanisms of motivated behaviour onto the tried-and-tested footing of the reflex theory and include the problem as a whole within the compass of the Pavlovian potent monistic teaching of higher nervous activity.

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### TO THE READER

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For Notes

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## The Learning Brain

Edited by E.A. Asratyan, P.V. Simonov

The book is devoted to the findings of research carried out at the Institute of Higher Nervous Activity and Neurophysiology (USSR Academy of Science), the thirtieth anniversary of whose founding was celebrated in 1980.

The papers are linked by the common theoretical position of their authors, who basing themselves on the work of Sechenov, Pavlov and Ukhtomsky, the fathers of Soviet physiology, employed the broad arsenal of modern experimental technique and mathematical data processing.

The general theme is physiological mechanisms of learning and memory, i.e. the processes of the elaboration, retention and realization of conditioned reflexes.

The original approach of the authors to the pressing problems of modern science about activity of the brain will make it interesting for a broad circle of readers.

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